

**Applicant:** **Astra Pharmaceuticals Ltd.**  
Home Park  
Kings Langley  
Herts WD4 8DH  
United Kingdom

**Title:** **NOVEL COMPOUNDS**

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**Inventors:** **Andrew Baxter**  
**Elizabeth Kinchin**  
**Roger Bonnert**  
**Fraser Hunt**  
**Paul Willis**  
**Rupert Austin**

## NOVEL COMPOUNDS

The present invention relates to certain thiazolopyrimidine compounds, processes and intermediates used in their preparation, pharmaceutical compositions containing them and their use in therapy.

The compound 2,7-diamino-5-methylmercapto-thiazolo[4,5-*d*]pyrimidine is known from J. Amer. Chem. Soc., 73, 4226 – 4227 (1951).

Chemokines play an important role in immune and inflammatory responses in various diseases and disorders, including asthma and allergic diseases, as well as autoimmune pathologies such as rheumatoid arthritis and atherosclerosis. These small secreted molecules are a growing superfamily of 8-14 kDa proteins characterised by a conserved four cysteine motif. The chemokine superfamily can be divided into two main groups exhibiting characteristic structural motifs, the Cys-X-Cys (C-X-C) and Cys-Cys (C-C) families. These are distinguished on the basis of a single amino acid insertion between the NH-proximal pair of cysteine residues and sequence similarity.

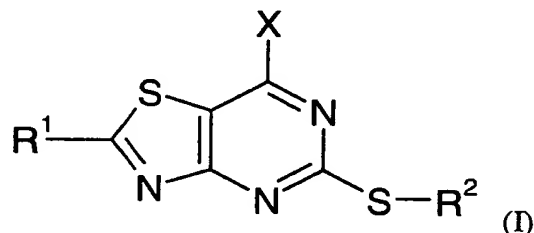
The C-X-C chemokines include several potent chemoattractants and activators of neutrophils such as interleukin-8 (IL-8) and neutrophil-activating peptide 2 (NAP-2).

The C-C chemokines include potent chemoattractants of monocytes and lymphocytes but not neutrophils such as human monocyte chemotactic proteins 1-3 (MCP-1, MCP-2 and MCP-3), RANTES (Regulated on Activation, Normal T Expressed and Secreted), eotaxin and the macrophage inflammatory proteins 1 $\alpha$  and 1 $\beta$  (MIP-1 $\alpha$  and MIP-1 $\beta$ ).

Studies have demonstrated that the actions of the chemokines are mediated by subfamilies of G protein-coupled receptors, among which are the receptors designated CCR1, CCR2, CCR2A, CCR2B, CCR3, CCR4, CCR5, CCR6, CCR7, CCR8, CCR9, CCR10, CXCR1, CXCR2, CXCR3 and CXCR4. These receptors represent good targets for drug

development since agents which modulate these receptors would be useful in the treatment of disorders and diseases such as those mentioned above.

In accordance with the present invention, there is therefore provided a compound of  
5 general formula

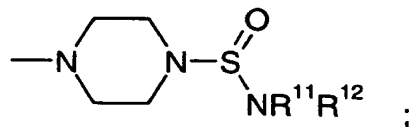


wherein  $R^1$  represents a hydrogen atom, or a group  $-NR^3R^4$ ;

$R^3$  and  $R^4$  each independently represent a hydrogen atom, or a 4-piperidiny,  $C_3$ - $C_6$

10 cycloalkyl or  $C_1$ - $C_8$  alkyl group, which latter two groups may be optionally substituted by one or more substituent groups independently selected from halogen atoms and  $-NR^5R^6$ ,  $-CONR^5R^6$ ,  $-OR^7$ ,  $-COOR^7$ ,  $-NR^8COR^9$ ,  $-SR^{10}$ ,  $-SO_2R^{10}$ ,  $-SO_2NR^5R^6$ ,  $-NR^8SO_2R^9$ , morpholinyl,  $C_1$ - $C_4$  alkyl,  $C_3$ - $C_6$  cycloalkyl, tetrahydrofuranyl and aryl groups, wherein an aryl substituent group may be a phenyl, naphthyl, thienyl, pyridinyl, imidazolyl or

15 indolyl group, each of which may be optionally substituted by one or more substituents independently selected from halogen atoms and cyano, nitro,  $-NR^5R^6$ ,  $-CONR^5R^6$ ,  $-OR^7$ ,  $-NR^8COR^9$ ,  $-SO_2NR^5R^6$ ,  $-NR^8SO_2R^9$ ,  $C_1$ - $C_6$  alkyl and trifluoromethyl groups, or  $R^3$  and  $R^4$  together with the nitrogen atom to which they are attached form a 4- to  
20 7-membered saturated heterocyclic ring system, which ring system may be optionally substituted by one or more substituent groups independently selected from



$-\text{NR}^5\text{R}^6$ ,  $-\text{CONR}^5\text{R}^6$ ,  $-\text{OR}^7$ ,  $-\text{COOR}^{10}$ ,  $-\text{NR}^8\text{COR}^9$ , and  $\text{C}_1\text{-C}_6$  alkyl optionally substituted by one or more substituents independently selected from halogen atoms and  $-\text{NR}^{11}\text{R}^{12}$  and  $-\text{OR}^7$  groups;

X represents a group  $-\text{OH}$  or  $-\text{NR}^{13}\text{R}^{14}$ ;

5  $\text{R}^{13}$  and  $\text{R}^{14}$  each independently represent a hydrogen atom, a 4-piperidinyl group optionally substituted by a  $\text{C}_1\text{-C}_4$  alkylphenyl substituent group, or a  $\text{C}_3\text{-C}_7$  carbocyclic,  $\text{C}_1\text{-C}_8$  alkyl,  $\text{C}_2\text{-C}_6$  alkenyl or  $\text{C}_2\text{-C}_6$  alkynyl group, which latter four groups may be optionally substituted by one or more substituent groups independently selected from halogen atoms and  $-\text{NR}^5\text{R}^6$ ,  $-\text{CONR}^5\text{R}^6$ ,  $-\text{OR}^7$ ,  $-\text{COOR}^7$ ,  $-\text{NR}^8\text{COR}^9$ ,  $-\text{SR}^{10}$ ,  
10  $-\text{SO}_2\text{R}^{10}$ ,  $-\text{SO}_2\text{NR}^5\text{R}^6$ ,  $-\text{NR}^8\text{SO}_2\text{R}^9$ , morpholinyl,  $\text{C}_1\text{-C}_4$  alkyl,  $\text{C}_3\text{-C}_6$  cycloalkyl and aryl groups, wherein an aryl substituent group may be a phenyl, naphthyl, thienyl, pyridinyl, imidazolyl or indolyl group, each of which may be optionally substituted by one or more substituents independently selected from halogen atoms and cyano, nitro,  $-\text{NR}^5\text{R}^6$ ,  $-\text{CONR}^5\text{R}^6$ ,  $-\text{OR}^7$ ,  $-\text{NR}^8\text{COR}^9$ ,  $-\text{SO}_2\text{NR}^5\text{R}^6$ ,  $\text{NR}^8\text{SO}_2\text{R}^9$ ,  $\text{C}_1\text{-C}_6$  alkyl and  
15 trifluoromethyl groups, or  $\text{R}^{13}$  and  $\text{R}^{14}$  together with the nitrogen atom to which they are attached form a 4- to 7-membered saturated heterocyclic ring system, which ring system may be optionally substituted by one or more substituent groups independently selected from  $-\text{NR}^5\text{R}^6$ ,  $-\text{CONR}^5\text{R}^6$ ,  $-\text{OR}^7$ ,  $-\text{COOR}^7$ ,  $-\text{NR}^8\text{COR}^9$ , and  $\text{C}_1\text{-C}_6$  alkyl optionally substituted by one or more substituents independently selected from halogen atoms and phenyl,  $-\text{NR}^{11}\text{R}^{12}$  and  $-\text{OR}^7$  groups;

$\text{R}^2$  represents a  $\text{C}_1\text{-C}_6$  alkyl or  $\text{C}_2\text{-C}_6$  alkenyl group optionally substituted by a phenyl or phenoxy group, wherein the phenyl or phenoxy group may itself be optionally substituted by one or more substituents independently selected from halogen atoms and nitro,

25  $\text{C}_1\text{-C}_6$  alkyl, trifluoromethyl,  $-\text{OR}^7$ ,  $-\text{C}(\text{O})\text{R}^7$ ,  $-\text{SR}^{10}$ ,  $-\text{NR}^{15}\text{R}^{16}$  and phenyl groups;  
 $\text{R}^5$  and  $\text{R}^6$  each independently represent a hydrogen atom or a  $\text{C}_1\text{-C}_6$  alkyl or phenyl group, each of which may be optionally substituted by one or more substituent groups independently selected from halogen atoms, phenyl,  $-\text{OR}^{17}$  and  $-\text{NR}^{15}\text{R}^{16}$ , or  
 $\text{R}^5$  and  $\text{R}^6$  together with the nitrogen atom to which they are attached form a 4- to

30 7-membered saturated heterocyclic ring system optionally comprising a further heteroatom

selected from oxygen and nitrogen atoms, which ring system may be optionally substituted by one or more substituent groups independently selected from phenyl,  $-OR^{17}$ ,  $-COOR^{17}$ ,  $-NR^{15}R^{16}$ ,  $-CONR^{15}R^{16}$ ,  $-NR^{15}COR^{16}$ ,  $-SONR^{15}R^{16}$ , and  $C_1$ - $C_6$  alkyl optionally substituted by one or more substituents independently selected from halogen atoms and  $-NR^{15}R^{16}$  and  $-OR^{17}$  groups;

$R^7$  and  $R^9$  each independently represent a hydrogen atom or a  $C_1$ - $C_6$ , particularly  $C_1$ - $C_4$ , alkyl (e.g. methyl, ethyl, propyl, butyl, pentyl or hexyl) or phenyl group, each of which may be optionally substituted by one or more (e.g. one, two, three or four) substituent groups independently selected from halogen atoms (e.g. fluorine, chlorine, bromine or iodine), phenyl,  $-OR^{17}$  and  $-NR^{15}R^{16}$ ; and

each of  $R^8$ ,  $R^{10}$ ,  $R^{11}$ ,  $R^{12}$ ,  $R^{15}$ ,  $R^{16}$  and  $R^{17}$  independently represents a hydrogen atom or a  $C_1$ - $C_6$ , particularly  $C_1$ - $C_4$ , alkyl (e.g. methyl, ethyl, propyl, butyl, pentyl or hexyl) or phenyl group; with the proviso that when  $R^1$  and X both represent  $-NH_2$ , then  $R^2$  does not represent a methyl group;

or a pharmaceutically acceptable salt or solvate thereof.

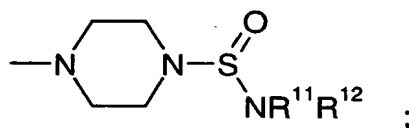
In the context of the present specification, unless otherwise indicated, an alkyl or alkenyl group or an alkyl or alkenyl moiety in a substituent group may be linear or branched.

Where a substituent in an alkenyl group is a phenoxy group, the phenoxy group is not attached to an unsaturated carbon atom. A carbocyclic group is a saturated hydrocarbyl group that may be monocyclic or polycyclic (e.g. bicyclic). Similarly, a saturated heterocyclic ring system may be monocyclic or polycyclic (e.g. bicyclic).

In formula (I) above, the group  $R^1$  represents a hydrogen atom, or a group  $-NR^3R^4$ . Particularly advantageous compounds of formula (I) are those in which  $R^1$  represents a group  $-NR^3R^4$ .

Preferably,  $R^3$  and  $R^4$  each independently represent a hydrogen atom, or a 4-piperidinyl,  $C_3$ - $C_6$  cycloalkyl (i.e. cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl) or  $C_1$ - $C_8$ , particularly  $C_1$ - $C_6$ , alkyl group (e.g. methyl, ethyl, propyl, isopropyl, butyl, isobutyl,

t-butyl, pentyl, hexyl, heptyl or octyl), which latter two groups may be optionally substituted by one, two, three or four substituent groups independently selected from halogen atoms (e.g. fluorine, chlorine, bromine or iodine) and  $-\text{NR}^5\text{R}^6$ ,  $-\text{CONR}^5\text{R}^6$ ,  $-\text{OR}^7$ ,  $-\text{COOR}^7$ ,  $-\text{NR}^8\text{COR}^9$ ,  $-\text{SR}^{10}$ ,  $-\text{SO}_2\text{R}^{10}$ ,  $-\text{SO}_2\text{NR}^5\text{R}^6$ ,  $-\text{NR}^8\text{SO}_2\text{R}^9$ , morpholinyl,  $\text{C}_1$ - $\text{C}_4$  alkyl (e.g. methyl, ethyl, propyl, isopropyl, butyl or t-butyl),  $\text{C}_3$ - $\text{C}_6$  cycloalkyl (i.e. cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl), tetrahydrofuranyl and aryl groups, wherein an aryl substituent group may be a phenyl, naphthyl, thienyl, pyridinyl, imidazolyl or indolyl group, each of which may be optionally substituted by one, two, three or four substituents independently selected from halogen atoms (e.g. fluorine, chlorine, bromine or iodine) and cyano, nitro,  $-\text{NR}^5\text{R}^6$ ,  $-\text{CONR}^5\text{R}^6$ ,  $-\text{OR}^7$ ,  $-\text{NR}^8\text{COR}^9$ ,  $-\text{SO}_2\text{NR}^5\text{R}^6$ ,  $-\text{NR}^8\text{SO}_2\text{R}^9$ ,  $\text{C}_1$ - $\text{C}_6$ , particularly  $\text{C}_1$ - $\text{C}_4$ , alkyl (e.g. methyl, ethyl, propyl, butyl, pentyl or hexyl) and trifluoromethyl groups, or  $\text{R}^3$  and  $\text{R}^4$  together with the nitrogen atom to which they are attached form a 4- to 7-membered saturated heterocyclic ring system, which ring system may be optionally substituted by one, two or three substituent groups independently selected from



$-\text{NR}^5\text{R}^6$ ,  $-\text{CONR}^5\text{R}^6$ ,  $-\text{OR}^7$ ,  $-\text{COOR}^{10}$ ,  $-\text{NR}^8\text{COR}^9$ , and  $\text{C}_1$ - $\text{C}_6$ , particularly  $\text{C}_1$ - $\text{C}_4$ , alkyl (e.g. methyl, ethyl, propyl, butyl, pentyl or hexyl) optionally substituted by one, two or three substituents independently selected from halogen atoms (e.g. fluorine, chlorine, bromine or iodine) and  $-\text{NR}^{11}\text{R}^{12}$  and  $-\text{OR}^7$  groups.

Particularly advantageous compounds of formula (I) are those in which  $\text{R}^3$  and  $\text{R}^4$  each independently represent a hydrogen atom, or a  $\text{C}_1$ - $\text{C}_6$  alkyl group substituted by a  $-\text{CONR}^5\text{R}^6$  or imidazolyl (e.g. 1*H*-imidazol-4-yl) group.

Preferably,  $\text{R}^2$  represents a  $\text{C}_1$ - $\text{C}_6$  alkyl or  $\text{C}_2$ - $\text{C}_6$  alkenyl group optionally substituted by a phenyl or phenoxy group, wherein the phenyl or phenoxy group may itself be optionally

substituted by one, two, three or four substituents independently selected from halogen atoms (e.g. fluorine, chlorine, bromine or iodine) and nitro, C<sub>1</sub>-C<sub>6</sub>, particularly C<sub>1</sub>-C<sub>4</sub>, alkyl (e.g. methyl, ethyl, propyl, butyl, pentyl or hexyl), trifluoromethyl, -OR<sup>7</sup>, -C(O)R<sup>7</sup>, -SR<sup>10</sup>, -NR<sup>15</sup>R<sup>16</sup> and phenyl groups.

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Particularly advantageous compounds of formula (I) are those in which R<sup>2</sup> represents a C<sub>1</sub>-C<sub>6</sub> alkyl group optionally substituted by a phenyl, halophenyl (e.g. 2,3-difluorophenyl) or -OR<sup>7</sup> (e.g. phenoxy) group.

- 10 Preferably, R<sup>5</sup> and R<sup>6</sup> each independently represent a hydrogen atom or a C<sub>1</sub>-C<sub>6</sub>, particularly C<sub>1</sub>-C<sub>4</sub>, alkyl or phenyl group, each of which may be optionally substituted by one, two, three or four substituent groups independently selected from halogen atoms (e.g. fluorine, chlorine, bromine or iodine), phenyl, -OR<sup>17</sup> and -NR<sup>15</sup>R<sup>16</sup>, or R<sup>5</sup> and R<sup>6</sup> together with the nitrogen atom to which they are attached form a 4- to
- 15 7-membered saturated heterocyclic ring system optionally comprising a further heteroatom selected from oxygen and nitrogen atoms (e.g. one or two oxygen and/or nitrogen atoms), which ring system may be optionally substituted by one, two or three substituent groups independently selected from phenyl, -OR<sup>17</sup>, -COOR<sup>17</sup>, -NR<sup>15</sup>R<sup>16</sup>, -CONR<sup>15</sup>R<sup>16</sup>, -NR<sup>15</sup>COR<sup>16</sup>, -SONR<sup>15</sup>R<sup>16</sup>, and C<sub>1</sub>-C<sub>6</sub>, particularly C<sub>1</sub>-C<sub>4</sub>, alkyl (e.g. methyl, ethyl,
- 20 propyl, butyl, pentyl or hexyl) optionally substituted by one, two or three substituents independently selected from halogen atoms (e.g. fluorine, chlorine, bromine or iodine) and -NR<sup>15</sup>R<sup>16</sup> and -OR<sup>17</sup> groups.

- Preferably, R<sup>13</sup> and R<sup>14</sup> each independently represent a hydrogen atom, a 4-piperidinyl
- 25 group optionally substituted by a C<sub>1</sub>-C<sub>4</sub> alkylphenyl substituent group, or a C<sub>3</sub>-C<sub>7</sub> carbocyclic, C<sub>1</sub>-C<sub>8</sub>, particularly C<sub>1</sub>-C<sub>6</sub>, alkyl (e.g. methyl, ethyl, propyl, isopropyl, butyl, isobutyl, t-butyl, pentyl, hexyl, heptyl or octyl), C<sub>2</sub>-C<sub>6</sub> alkenyl (ethenyl, propenyl, butenyl, pentenyl or hexenyl) or C<sub>2</sub>-C<sub>6</sub> alkynyl (ethynyl, propynyl, butynyl, pentynyl or hexynyl) group, which latter four groups may be optionally substituted by one, two, three or four
- 30 substituent groups independently selected from halogen atoms (e.g. fluorine, chlorine,

bromine or iodine) and  $-NR^5R^6$ ,  $-CONR^5R^6$ ,  $-OR^7$ ,  $-COOR^7$ ,  $-NR^8COR^9$ ,  $-SR^{10}$ ,  $-SO_2R^{10}$ ,  $-SO_2NR^5R^6$ ,  $-NR^8SO_2R^9$ , morpholinyl,  $C_1$ - $C_4$  alkyl (e.g. methyl, ethyl, propyl, isopropyl, butyl or t-butyl),  $C_3$ - $C_6$  cycloalkyl (i.e. cyclopropyl, cyclobutyl, cyclopentyl or cyclohexyl), and aryl groups, wherein an aryl substituent group may be a phenyl, naphthyl, thienyl, pyridinyl, imidazolyl or indolyl group, each of which may be optionally substituted by one, two, three or four substituents independently selected from halogen atoms (e.g. fluorine, chlorine, bromine or iodine) and cyano, nitro,  $-NR^5R^6$ ,  $-CONR^5R^6$ ,  $-OR^7$ ,  $-NR^8COR^9$ ,  $-SO_2NR^5R^6$ ,  $NR^8SO_2R^9$ ,  $C_1$ - $C_6$ , particularly  $C_1$ - $C_4$ , alkyl (e.g. methyl, ethyl, propyl, butyl, pentyl or hexyl) and trifluoromethyl groups, or  $R^{13}$  and  $R^{14}$  together with the nitrogen atom to which they are attached form a 4- to 7-membered saturated heterocyclic ring system, which ring system may be optionally substituted by one, two or three substituent groups independently selected from  $-NR^5R^6$ ,  $-CONR^5R^6$ ,  $-OR^7$ ,  $-COOR^7$ ,  $-NR^8COR^9$ , and  $C_1$ - $C_6$ , particularly  $C_1$ - $C_4$ , alkyl (e.g. methyl, ethyl, propyl, butyl, pentyl or hexyl) optionally substituted by one, two or three substituents independently selected from halogen atoms (e.g. fluorine, chlorine, bromine or iodine) and phenyl,  $-NR^{11}R^{12}$  and  $-OR^7$  groups;

Particularly advantageous compounds of formula (I) are those in which one of  $R^{13}$  and  $R^{14}$  represents a hydrogen atom and the other of  $R^{13}$  and  $R^{14}$  represents a  $C_1$ - $C_6$  alkyl group substituted by an  $-OR^7$  group, e.g.  $-CH(CH_2CH_3)CH_2OH$ ,  $-C(CH_3)_2CH_2OH$  or  $CH(CH_2CH(CH_3)_2)CH_2OH$ .

Particularly preferred compounds of the invention include:

(2*R*)-2-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol,  
 (2*S*)-2-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol,  
 2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 5-[[[(3-Phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 (±)-2-[[2-Amino-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol,  
 2-[[2-Amino-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7-yl]amino]ethanol,



- 5-(Pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-Amino-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-[[3-(Dimethylamino)propyl]amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 5 2-[[2-(Diethylamino)ethyl]amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-[[2-(Dimethylamino)ethyl]amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-[(3-Hydroxypropyl)amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-[[2-(Acetylamino)ethyl]amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 (±)-2-[(2,3-Dihydroxypropyl)amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 10 2-[[2-(4-Morpholinyl)ethyl]amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-[(2-Methoxyethyl)amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-[(1-Methylethyl)amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-(Cyclopropylamino)-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 (±)-2-[(2-Hydroxypropyl)amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 15 2-[[2-(2-Hydroxyethoxy)ethyl]amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-[(2-Hydroxy-2-methylpropyl)amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-[(2-Hydroxyethyl)amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 (2*S*,3*R*)-3-Hydroxy-2-[(7-oxo-5-(pentylthio)-4*H*-thiazolo[4,5-*d*]pyrimidin-2-yl)-  
 amino]butanamide,  
 20 *N*<sup>7</sup>-[3-(Dimethylamino)propyl]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine,  
*N*<sup>7</sup>-[2-(Diethylamino)ethyl]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine,  
*N*<sup>7</sup>-[2-(Dimethylamino)ethyl]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine,  
 3-[(2-Amino-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-1-propanol,  
*N*<sup>7</sup>-Cyclohexyl-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine,  
 25 (±)-3-[(2-Amino-5-((phenylmethyl)thio)thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-1,2-  
 propanediol,  
*N*<sup>7</sup>-(2-Methoxyethyl)-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine,  
 5-(Pentylthio)-*N*<sup>7</sup>-propylthiazolo[4,5-*d*]pyrimidine-2,7-diamine,  
*N*<sup>7</sup>-Cyclopentyl-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine,  
 30 *N*<sup>7</sup>-Cyclopropyl-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine,

- $N^7$ -(2-Methylpropyl)-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine,  
 (±)-1-[(2-Amino-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-2-propanol,  
 (exo)- $N^7$ -Bicyclo[2.2.1]hept-2-yl-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine,  
 2-[2-[(2-Amino-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7-yl)amino]ethoxy]ethanol,  
 5 (±)- $N^7$ -(2-Methylbutyl)-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine,  
 1-[(2-Amino-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-2-methyl-2-propanol,  
 $N^7$ -(2-Aminophenyl)methyl]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine,  
 2-Amino-5-[(2-phenoxyethyl)thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 (*E*)-2-Amino-5-[(3-phenyl-2-propenyl)thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 10 2-Amino-5-[[3-[2,4-bis(1,1-dimethylethyl)phenoxy]propyl]thio]thiazolo[4,5-*d*]pyrimidin-  
 7(4*H*)-one,  
 2-Amino-5-[[[(4-trifluoromethyl)phenyl]methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-Amino-5-[[[(3,5-dichlorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-Amino-5-[[[(2,4-dichlorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 15 2-Amino-5-[[[(3,4-dichlorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-Amino-5-[[[(3,5-dibromophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-Amino-5-[[[(2-nitrophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-Amino-5-[[[(2-fluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-Amino-5-[[[(2-iodophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 20 2-Amino-5-[[[(3-chlorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-Amino-5-[[[(2-chlorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-Amino-5-[[[(4-chloro-2-nitrophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-Amino-5-[[[(3-chloro-4-methoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-Amino-5-[[[(2,3-dichlorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 25 2-Amino-5-[[[(3,5-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-Amino-5-[[[(2,4-bis(trifluoromethyl)phenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-  
 one,  
 2-Amino-5-[[[(2-bromophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 2-Amino-5-[[[(2,3,4-trifluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
 30 2-Amino-5-[[[(3-bromophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,

2-Amino-5-[[2-fluoro-3-methylphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,  
3-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2,2-dimethyl-1-  
propanol,

(±)-α-[[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-  
5 yl]amino]methyl]benzenemethanol,

(*R*)-β-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-  
yl]amino]benzenepropanol,

2-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]ethanol,

(2*R*)-2-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]4-  
10 methylpentanol,

(±)-1-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-propanol,

(±)-β-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-4-  
chlorobenzenepropanol,

(±)-3-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1,2-  
15 propanediol,

2-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]propylamino]ethanol,

(±)-1-[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-3-pyrrolidinol,

(±)-1-[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-3-piperidinol,

1-[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-4-piperidinol,

20 3-[[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2,2-  
dimethyl-1-propanol,

(±)-2-[[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-  
1-butanol,

(±)-α-[[[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-  
25 amino]methyl]benzenemethanol,

4-[[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-  
butanol,

6-[[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-  
hexanol,

4-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-amino]cyclohexanol,

(*R*)-β-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-amino]benzenepropanol,

5 (±)-2-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

2-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-amino]ethanol,

(2*R*)-2-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-amino]-4-methylpentanol,

(±)-1-Amino-3-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-propanol,

(±)-1-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-propanol,

15 2-[[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]methyl]-2-ethyl-1,3-propanediol,

(±)-β-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-4-chlorobenzenepropanol,

(±)-3-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1,2-propanediol,

2-[[2-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]ethyl]amino]ethanol,

3-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

25 (±)-α-[[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]methyl]-3,4-dichlorobenzenepropanol,

1-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-2-propanol,

2-[[2-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]ethoxy]ethanol,

4-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-amino]cyclohexanol,

5-[[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-pentanol,

(2*S*)-2-[[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-4-(methylthio)-1-butanol,

5 2-[[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]butylamino]ethanol,

2-[[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]propylamino]ethanol,

2,2'-[[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]imino]bisethanol,

2-[[[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-(2-hydroxyethyl)amino]methyl]phenol,

3-[[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-(2-hydroxyethyl)amino]-1-propanol,

15 (±)-1-[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-3-pyrrolidinol,

(*trans*)-1-[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-4-hydroxy-*L*-proline phenylmethyl ester,

20 (±)-1-[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-3-piperidinemethanol,

(±)-1-[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-3-piperidinol,

(2*S*)-1-[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-2-pyrrolidinemethanol,

25 1-[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-4-piperidinol,

(2*R*)-2-[[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol,

30 (2*S*)-2-[[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol,

(2*R*)-2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol,

2-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1,3-propanediol,

5 2-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

10 1-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-2-propanol,

5-[[[(2,3-Difluorophenyl)methyl]thio]-*N*<sup>7</sup>-(2-fluoroethyl)thiazolo[4,5-*d*]pyrimidine-2,7-diamine,

(1*R-trans*) 2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-cyclopentanol,

15 (1*S-trans*) 2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-cyclopentanol,

2-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

20 2-Methyl-2-[[2-(methylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

2-[[2-[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[(phenylmethyl)amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

5-[[[(2,3-Difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,

25 (±)-2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol,

(1*S,2S*)-2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-cyclohexanol,

(±)-2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-ethanol.

(2*R*)-2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-4-methyl-1-pentanol,

5 (±)-1-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-propanol,

2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1,3-propanediol,

1-[[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]methyl]-cyclohexanol,

(2*R*)-2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol,

2-[[2-Amino-5-[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-(2-aminoethyl)amino]-1-ethanol.

15 2-[2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]ethoxy]-1-ethanol,

( $\alpha S$ )- $\alpha$ -[(1*R*)-1-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]methylamino]ethyl]-benzenemethanol,

1-[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-4-  
20 piperidinol,

5-[[*(2,3-Difluorophenyl)methyl*]thio]-*N*<sup>7</sup>-ethyl-thiazolo[4,5-*d*]pyrimidin-2,7-diamine,

5-[[*(2,3-Difluorophenyl)methyl*thio]-*N*<sup>7</sup>-(2-propenyl)-thiazolo[4,5-*d*]pyrimidine-2,7-diamine,

(1*S*,2*S*)-2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-phenyl-1,3-propanediol,

2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1,3-propanediol,

2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-ethanol.

(±)-5-[[[(2,3-Difluorophenyl)methyl]thio]-*N*<sup>7</sup>-(2-methoxy-1-methylethyl)-thiazolo[4,5-*d*]pyrimidine-2,7-diamine,

*N*<sup>7</sup>-Cyclopropyl-5-[[[(2,3-difluorophenyl)methyl]thio]-thiazolo[4,5-*d*]pyrimidine-2,7-diamine,

5 (±)-2-[[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]-thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

4-[[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]-thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol,

5-[[[(2,3-Difluorophenyl)methyl]thio]-*N*<sup>7</sup>-[2-(1*H*-imidazol-4-yl)ethyl]-thiazolo[4,5-*d*]pyrimidine-2,7-diamine,

10 (±)-*N*-[5-[[[(2,3-Difluorophenyl)methyl]thio]-7-[(2-hydroxy-1,1-dimethylethyl)amino]thiazolo[4,5-*d*]pyrimidin-2-yl]-serine, methyl ester,

2-[[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[(1-methylethyl)amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

15 2-[[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-(ethylamino)thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

2-[[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[[2-(1*H*-indol-3-yl)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

2-[[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[(1-naphthalenylmethyl)amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

2-[[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[(1,2-diphenylethyl)amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

2-[[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[(2,2,2-trifluoroethyl)amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

25 2-[[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[(3,4,5-trimethoxyphenyl)methyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

2-[[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[(1,1-dimethylethyl)amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,



2-[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[[2-(2-thienyl)ethyl]amino]thiazolo[4,5-  
d]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

2-[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[(4-methylcyclohexyl)amino]thiazolo[4,5-  
d]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

5 2-[[5-[[[(2,3-Difluorophenyl)methyl]thio]-7-[(2-hydroxy-1,1-  
dimethylethyl)amino]thiazolo[4,5-d]pyrimidin-2-yl]amino]-acetamide,

2-[[2-[[2-(4-Aminophenyl)ethyl]amino]-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-  
d]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

2-[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[(2-fluoroethyl)amino]thiazolo[4,5-  
10 d]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

2-[[2-(Cyclopropylamino)-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-d]pyrimidin-7-  
yl]amino]-2-methyl-1-propanol,

(±)-2-[[5-[[[(2,3-Difluorophenyl)methyl]thio]-7-[(2-hydroxy-1,1-  
dimethylethyl)amino]thiazolo[4,5-d]pyrimidin-2-yl]amino]-1-pentanol,

15 2-[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[[2-(2-  
hydroxyethoxy)ethyl]amino]thiazolo[4,5-d]pyrimidin-7-yl]amino]-2-methyl-1-propanol,  
N-[5-[[[(2,3-Difluorophenyl)methyl]thio]-6,7-dihydro-7-oxo-thiazolo[4,5-d]pyrimidin-2-  
yl]-DL-serine, methyl ester,

5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[(1-methylethyl)amino]-thiazolo[4,5-d]pyrimidin-  
20 7(4H)-one,

5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[[2-(1H-indol-3-yl)ethyl]amino]-thiazolo[4,5-  
d]pyrimidin-7(4H)-one,

2-[[5-[[[(2,3-Difluorophenyl)methyl]thio]-6,7-dihydro-7-oxo-thiazolo[4,5-d]pyrimidin-2-  
yl]amino]-acetamide,

25 2-[[2-(4-Aminophenyl)ethyl]amino]-5-[[[(2,3-difluorophenyl)methyl]thio]-thiazolo[4,5-  
d]pyrimidin-7(4H)-one,

5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[(2-fluoroethyl)amino]-thiazolo[4,5-d]pyrimidin-  
7(4H)-one,

5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[[2-(2-hydroxyethoxy)ethyl]amino]-thiazolo[4,5-  
30 d]pyrimidin-7(4H)-one,

2-[[2-(Cyclohexylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

2-[[2-[(1,1-Dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

5 *N*-[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]-DL-alanine, methyl ester,

4-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-cyclohexanol,

2-Methyl-2-[[2-[(4-phenylbutyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

2-Methyl-2-[[5-[(phenylmethyl)thio]-2-[[[(tetrahydro-2-furanyl)methyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

2-Methyl-2-[[2-[(1-methylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

15 2-[[2-[[2-(4-Aminophenyl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

*N*-[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]-L-valine, ethyl ester,

(2*S*)-2-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-4-methyl-pentanamide,

2-Methyl-2-[[2-[(2-phenylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

2-[[2-[[4-Aminophenyl)methyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

25 2-Methyl-2-[[5-[(phenylmethyl)thio]-2-[[2-(2-thienyl)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

2-[[2-[(2-Fluoroethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

2-Methyl-2-[[2-[[3-nitrophenyl)methyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

( $\alpha R$ )- $\alpha$ -[(1*S*)-1-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-

[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-benzenemethanol,

2-Methyl-2-[[5-[(phenylmethyl)thio]-2-[(3,4,5-

trimethoxyphenyl)methyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

5 2-Methyl-2-[[2-[(1*R*-trans)-(2-phenylcyclopropyl)amino]-5-

[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

2-[[2-[[2-(1*H*-Indol-3-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

2-[[2-[(1,1-Dimethylpropyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-

10 yl]amino]-2-methyl-1-propanol,

( $\pm$ )-2-Methyl-2-[[2-[(1-methylbutyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

( $\pm$ )-2-Methyl-2-[[2-[(1-methylhexyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

15 2-[[2-[[2-(2-Aminophenyl)methyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

2-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-1,3-propanediol,

2-[[2-[[2-(Ethylthio)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

20 (2*S*)-2-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-3,3-dimethyl-1-butanol,

( $\alpha S$ )- $\alpha$ -[(1*R*)-1-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-

[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-2-methoxyethyl]-

25 benzenemethanol,

2-[[2-(Ethylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

2-[[2-[[[3-Fluoro-5-(trifluoromethyl)phenyl]methyl]amino]-5-

[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

(±)-2-Methyl-2-[[2-[(1-methylpropyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-  
d]pyrimidin-7-yl]amino]-1-propanol,

2-[[2-[(4-Methoxyphenyl)methyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-d]pyrimidin-  
7-yl]amino]-2-methyl-1-propanol,

5 2-[[2-[(2-Hydroxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-d]pyrimidin-7-  
yl]amino]-2-methyl-1-propanol,

2-[[2-[(1*H*-Imidazol-4-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-d]pyrimidin-  
7-yl]amino]-2-methyl-1-propanol,

10 2-[[2-[(Diphenylmethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-d]pyrimidin-7-  
yl]amino]-2-methyl-1-propanol,

(2*S*)-2-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-  
d]pyrimidin-2-yl]amino]-1-butanol,

2-[[2-[(2,2-Diethoxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-d]pyrimidin-7-  
yl]amino]-2-methyl-1-propanol,

15 4-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-  
d]pyrimidin-2-yl]amino]-1-butanol,

(1*S*,2*S*)-2-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-  
d]pyrimidin-2-yl]amino]-cyclohexanol,

20 (±)-2-[[2-[(2-Hydroxy-1-methylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-  
d]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

2-[[2-[[2-(2-Hydroxyethoxy)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-d]pyrimidin-  
7-yl]amino]-2-methyl-1-propanol,

(±)-2-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-  
d]pyrimidin-2-yl]amino]-1-pentanol,

25 2-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-  
d]pyrimidin-2-yl]amino]-acetamide,

(±)-2-[[2-[[1-(4-Fluorophenyl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-  
d]pyrimidin-7-yl]amino]-2-methyl-propanol,

30 (1*R*,2*S*)-2-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-  
d]pyrimidin-2-yl]amino]-cyclohexanol,

( $\alpha S$ )- $\alpha$ -[(1*R*)-1-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-

[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-benzenemethanol,

( $\pm$ )-2-[[2-(Methylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

5 (2*R*)-4-Methyl-2-[[2-(methylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-pentanol,

*N*-[2-(Methylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-L-serine, ethyl ester,

( $\pm$ )-2-[[5-[(Phenylmethyl)thio]-2-[[[(tetrahydro-2-furanyl)methyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol,

10 ( $\pm$ )-2-[[5-[(Phenylmethyl)thio]-2-[[[(tetrahydro-2-furanyl)methyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

(2*R*)-4-Methyl-2-[[5-[(phenylmethyl)thio]-2-[[[(tetrahydro-2-furanyl)methyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-pentanol,

15 *N*-[5-[(Phenylmethyl)thio]-2-[[[(tetrahydro-2-furanyl)methyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]-L-serine, ethyl ester,

( $\pm$ )-2-[[2-[[2-(2-Hydroxyethoxy)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

( $\pm$ )-4-[2-[[7-[[1-(Hydroxymethyl)propyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-benzenesulfonamide,

20 ( $\pm$ )-4-[2-[[7-[(2-Hydroxy-1-methylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-benzenesulfonamide,

4-[2-[[7-[[1-*R*)-1-(Hydroxymethyl)-3-methylbutyl]amino]-5-

[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-benzenesulfonamide,

25 ( $\pm$ )-4-[2-[[7-[(2-Hydroxypropyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-benzenesulfonamide,

*N*<sup>7</sup>-Ethyl-*N*<sup>2</sup>-[2-(1*H*-imidazol-4-yl)ethyl]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidine-2,7-diamine,

*N*<sup>2</sup>-[2-(1*H*-Imidazol-4-yl)ethyl]-5-[(phenylmethyl)thio]-*N*<sup>7</sup>-(3-pyridinylmethyl)-

30 thiazolo[4,5-*d*]pyrimidine-2,7-diamine,

(±)-2-[[2-[[2-(1*H*-Imidazol-4-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol,

(±)-2-[[2-[[2-(1*H*-Imidazol-4-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

5 (2*R*)-2-[[2-[[2-(1*H*-Imidazol-4-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-4-methyl-1-pentanol,

(±)-1-[[2-[[2-(1*H*-Imidazol-4-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-propanol,

10 5-[[2-[[2-(1*H*-Imidazol-4-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-pentanol,

1-[2-[[2-(1*H*-Imidazol-4-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-4-(phenylmethyl)-4-piperidinol,

(±)-1-[2-[[2-(1*H*-Imidazol-4-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-3-piperidinecarboxamide,

15 2-[Ethyl[2-[[2-(1*H*-imidazol-4-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-ethanol,

*N*<sup>2</sup>-[2-(1*H*-Imidazol-4-yl)ethyl]-*N*<sup>7</sup>,*N*<sup>7</sup>-dimethyl-5-[(phenylmethyl)thio]-thiazolo[4,5-*d*]pyrimidine-2,7-diamine,

*N*<sup>7</sup>-[2-(Diethylamino)ethyl]-*N*<sup>7</sup>-ethyl-*N*<sup>2</sup>-[2-(1*H*-imidazol-4-yl)ethyl]-5-

20 [(phenylmethyl)thio]-thiazolo[4,5-*d*]pyrimidine-2,7-diamine,

*N*<sup>2</sup>-(2-Phenoxyethyl)-5-[(phenylmethyl)thio]-*N*<sup>7</sup>-(3-pyridinylmethyl)-thiazolo[4,5-*d*]pyrimidine-2,7-diamine,

*N*<sup>2</sup>-(2-Phenoxyethyl)-*N*<sup>7</sup>-[1-(phenylmethyl)-4-piperidinyl]-5-[(phenylmethyl)thio]-thiazolo[4,5-*d*]pyrimidine-2,7-diamine,

25 2-Methyl-2-[[2-[(2-phenoxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

(±)-2-[[2-[(2-Phenoxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

30 (±)-4-Methyl-2-[[2-[(2-phenoxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-pentanol,

1-[2-[(2-Phenoxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-4-(phenylmethyl)-4-piperidinol,

2-[[2-(Cyclopropylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol,

5 2-[[2-(Cyclopropylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

(2*R*)-2-[[2-(Cyclopropylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-4-methyl-1-pentanol,

10 *N*-[2-(Cyclopropylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-L-serine, ethyl ester,

(2*R*)-2-[[2-[[1-(Hydroxymethyl)butyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-4-methyl-1-pentanol,

*N*-[2-[[1-(Hydroxymethyl)butyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-L-serine, ethyl ester,

15 (±)-2-[[7-[Cyclohexyl(2-hydroxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-1-pentanol,

2-[2-[[7-(Ethylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethoxy]-1-ethanol,

20 2-[2-[[7-[(1-Methylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethoxy]-1-ethanol,

(±)-2-[[2-[[2-(2-Hydroxyethoxy)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol,

2-[[2-[[2-(2-Hydroxyethoxy)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol,

25 (2*R*)-2-[[2-[[2-(2-Hydroxyethoxy)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-4-methyl-1-pentanol,

2-[Cyclohexyl-2-[[2-(2-hydroxyethoxy)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-ethanol,

30 (±)-2-[[5-[(Phenylmethyl)thio]-2-(4-piperidinylamino)thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

(±)-*N*-[2-[[7-[[1-(Hydroxymethyl)propyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-acetamide,

(±)-*N*-[2-[[7-[(2-Hydroxy-1-methylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-acetamide,

5 *N*-[2-[[7-[(2-Hydroxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-acetamide,

*N*-[2-[[7-[(1*R*)-1-(Hydroxymethyl)-3-methylbutyl]amino]-5-

[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-acetamide,

10 *N*<sup>7</sup>-(2-Methoxyethyl)-5-[(phenylmethyl)thio]-*N*<sup>2</sup>-[2-(2-thienyl)ethyl]thiazolo[4,5-*d*]pyrimidine-2,7-diamine,

*N*<sup>7</sup>-(2-Ethoxyethyl)-5-[(phenylmethyl)thio]-*N*<sup>2</sup>-[2-(2-thienyl)ethyl]thiazolo[4,5-*d*]pyrimidine-2,7-diamine,

*N*<sup>7</sup>-(2,2-Dimethylpropyl)-5-[(phenylmethyl)thio]-*N*<sup>2</sup>-[2-(2-thienyl)ethyl]thiazolo[4,5-*d*]pyrimidine-2,7-diamine,

15 (2*R*)-4-Methyl-2-[[5-[(phenylmethyl)thio]-2-[[2-(2-thienyl)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-pentanol,

(±)-1-[[5-[(Phenylmethyl)thio]-2-[[2-(2-thienyl)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-propanol,

20 (±)-2-[[5-[(Phenylmethyl)thio]-2-[[2-(2-thienyl)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol,

(±)-2-[[5-[(Phenylmethyl)thio]-2-[[2-(2-thienyl)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

(2*R*)-2-[[2-[(2-Hydroxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-4-methyl-1-pentanol,

25 (±)-*N,N*-Diethyl-1-[2-[(2-hydroxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-3-piperidinecarboxamide,

(2*R*)-2-[[2-[(3-Hydroxypropyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-4-methyl-1-pentanol,

30 (±)-2-[[2-[(3-Hydroxypropyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol,



(±)-2-[[2-[(3-Hydroxypropyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

2-[[7-[(2-Hydroxy-1-methylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-acetamide,

5 4-[1-[7-[(4-Methylcyclohexyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]-3-azetidiny]-1-piperazinesulfonamide,

3-[[2-[[2-(4-Morpholinyl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

2-Methyl-2-[[2-[[2-(4-morpholinyl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

(±)-2-[[2-[[2-(4-Morpholinyl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol,

(2*R*)-4-Methyl-2-[[2-[[2-(4-morpholinyl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-pentanol,

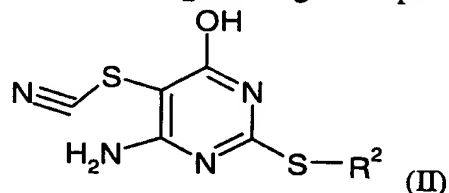
15 2-[[2-(3,4-Dihydroxyphenyl)ethyl]amino]-5-[(phenylmethyl)thio]-thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,

(±)-2-[(2-Hydroxy-1-methylethyl)amino]-5-[(phenylmethyl)thio]-thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one,

and their pharmaceutically acceptable salts and solvates.

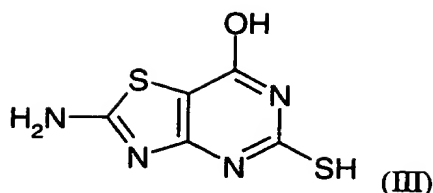
20 According to the invention there is also provided a process for the preparation of a compound of formula (I) which comprises:

(a) when X represents -OH and R<sup>1</sup> is NH<sub>2</sub>, heating a compound of general formula



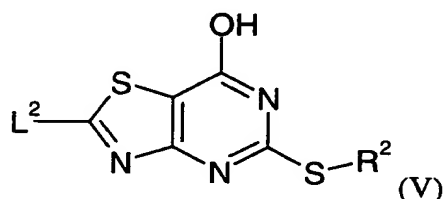
25 wherein R<sup>2</sup> is as defined in formula (I); or

(b) when X represents -OH and R<sup>1</sup> is NH<sub>2</sub>, reacting a compound of formula



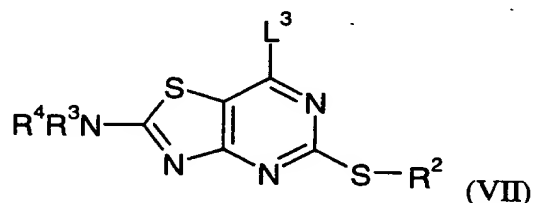
with a compound of general formula (IV),  $R^2 - L^1$ , wherein  $L^1$  represents a leaving group such as a halogen atom (e.g. chlorine) and  $R^2$  is as defined in formula (I); or

- (c) when X represents  $-OH$  or  $-NR^{13}R^{14}$  and  $R^1$  is a hydrogen atom, reacting a  
 5 corresponding compound of formula (I) in which  $R^1$  is  $NH_2$ , with a diazotizing agent; or  
 (d) when X represents  $-OH$  and  $R^1$  is a group  $-NR^3R^4$ , reacting a compound of general formula

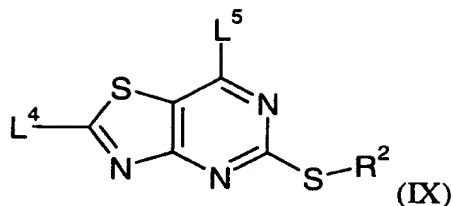


- wherein  $L^2$  represents a leaving group such as a halogen atom (e.g. bromine) and  $R^2$  is as  
 10 defined in formula (I), with a compound of general formula (VI),  $R^3R^4NH$ , wherein  $R^3$  and  $R^4$  are as defined in formula (I); or

(e) when X represents  $-NR^{13}R^{14}$  and  $R^1$  represents  $-NR^3R^4$ , reacting a compound of general formula



- 15 wherein  $L^3$  represents a leaving group such as a halogen atom (e.g. chlorine) and  $R^2$ ,  $R^3$  and  $R^4$  are as defined in formula (I), with a compound of general formula (VIII),  $NHR^{13}R^{14}$ , wherein  $R^{13}$  and  $R^{14}$  are as defined in formula (I); or  
 (f) when X represents  $-NR^{13}R^{14}$  and  $R^1$  represents  $-NR^3R^4$ , reacting a compound of general formula



wherein  $L^4$  is a leaving group (e.g. bromine),  $L^5$  is a leaving group (e.g. chlorine) and  $R^2$  is as defined in formula (I), initially with a compound of formula (VI) as defined in (d) above followed by reaction with a compound of formula (VIII) as defined in (e) above;

and optionally after (a), (b), (c), (d), (e) or (f) forming a pharmaceutically acceptable salt or solvate of the compound of formula (I).

Process (a) is conveniently carried out in the presence of a solvent or solvent mixture such as dimethylformamide/water at a temperature in the range from e.g. 50 to 150°C.

Process (b) is conveniently carried out in an organic solvent such as tetrahydrofuran or dimethyl sulphoxide/dimethylformamide mixture, optionally in the presence of a base such as potassium *tert*-butoxide or diisopropylamide.

Process (c) is conveniently carried out in an organic solvent such as tetrahydrofuran.

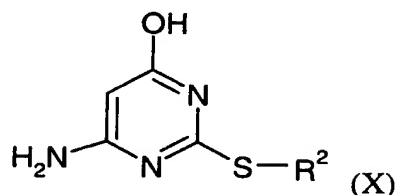
Examples of suitable diazotizing agents to use include *tert*-butyl nitrite.

Process (d) is conveniently carried out in an organic solvent such as tetrahydrofuran, e.g. at a temperature of 50°C for 5 hours.

Process (e) is conveniently carried out in an organic solvent such as tetrahydrofuran with heating for a period in the range from 1 day to 3 weeks.

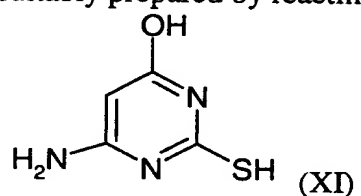
Process (f) is conveniently carried out in an organic solvent such as tetrahydrofuran or N-methylpyrrolidine at a temperature between 0° and 130°C, with a reaction time of 1 hour to 3 weeks.

Compounds of formula (II) may be readily prepared by reacting a compound of general formula



- 5 wherein  $R^2$  is as defined above, with potassium thiocyanate and bromine in dimethylformamide/pyridine.

Compounds of formula (X) are suitably prepared by reacting a compound of formula



- 10 with a compound of formula (IV) as defined above.

Compounds of formula (V) may be prepared by reacting a compound of formula (I) in which  $R^1$  is  $NH_2$ , with a diazotizing agent and a halogenating agent. The reaction is conveniently carried out in an organic solvent such as acetonitrile in the presence of a

15 diazotizing agent such as *tert*-butyl nitrite and a halogenating agent such as a trimethylsilyl halide.

Compounds of formula (VII) in which  $L^3$  is a chlorine atom may be prepared by reacting a compound of formula (I) in which X is -OH with phosphorus oxychloride in

20 dimethylaniline under reflux conditions.

Compounds of formula (IX) in which  $L^4$  represents a bromine atom and  $L^5$  represents a chlorine atom may be prepared by reacting a compound of formula (I) in which X is -OH and  $R^1$  is  $NH_2$  with phosphorus oxychloride in dimethylaniline under reflux conditions,

25 followed by reaction with *tert*-butyl nitrite and bromoform.

Compounds of formulae (III), (IV), (VI), (VIII) and (XI) are either commercially available, are well known in the literature or may be prepared easily using known techniques.

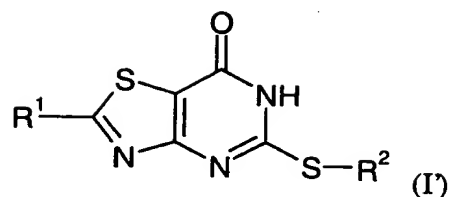
5 The compounds of formulae (V), (VII) and (IX) are novel intermediates and therefore form a further aspect of the present invention. In formula (V),  $L^2$  is preferably a bromine atom. In formula (VII),  $R^3$  and  $R^4$  preferably both represent a hydrogen atom. In formula (IX),  $L^3$  is preferably a bromine atom and  $L^4$  is preferably a chlorine atom.

10 It will be appreciated by those skilled in the art that in the processes of the present invention certain functional groups such as hydroxyl or amino groups in the starting reagents or intermediate compounds may need to be protected by protecting groups. Thus, the preparation of the compounds of formula (I) may involve, at an appropriate stage, the removal of one or more protecting groups.

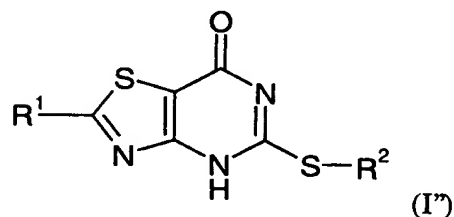
15 The protection and deprotection of functional groups is fully described in 'Protective Groups in Organic Chemistry', edited by J. W. F. McOmie, Plenum Press (1973), and 'Protective Groups in Organic Synthesis', 2nd edition, T. W. Greene & P. G. M. Wuts, Wiley-Interscience (1991).

20 The compounds of formula (I) above may be converted to a pharmaceutically acceptable salt or solvate thereof, preferably an acid addition salt such as a hydrochloride, hydrobromide, phosphate, acetate, fumarate, maleate, tartrate, citrate, oxalate, methanesulphonate or *p*-toluenesulphonate.

25 Certain compounds of formula (I) are capable of existing in stereoisomeric forms. It will be understood that the invention encompasses all geometric and optical isomers of the compounds of formula (I) and mixtures thereof including racemates. Tautomers and mixtures thereof also form an aspect of the present invention, for example tautomers of  
30 general formula

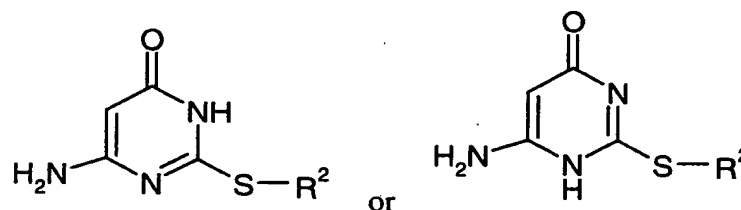
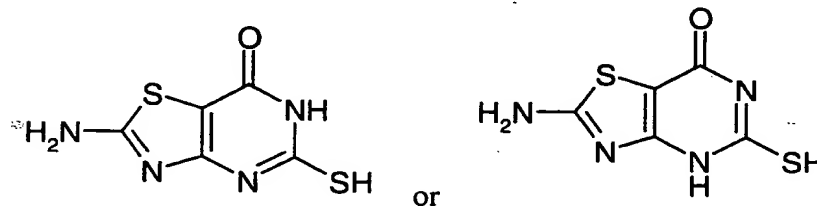
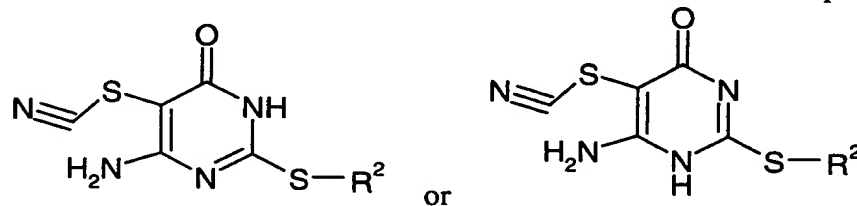


wherein  $R^1$  and  $R^2$  are as defined in formula (I), or of general formula

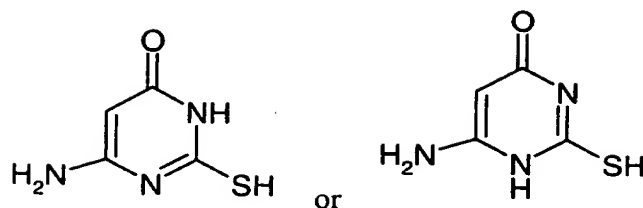


wherein  $R^1$  and  $R^2$  are as defined in formula (I).

Similarly, it will be understood that in the above processes tautomeric forms of the compounds of formulae (II), (III), (IX) and (X) may also be used, for example,



and



The compounds of formula (I) have activity as pharmaceuticals, in particular as modulators of chemokine receptor (especially CXCR2) activity, and may be used in the treatment (therapeutic or prophylactic) of conditions/diseases in human and non-human animals which are exacerbated or caused by excessive or unregulated production of chemokines. Examples of such conditions/diseases include:

- (1) **(the respiratory tract)** obstructive airways diseases including chronic obstructive pulmonary disease (COPD) such as irreversible COPD; asthma, such as bronchial, allergic, intrinsic, extrinsic and dust asthma, particularly chronic or inveterate asthma (e.g. late asthma and airways hyper-responsiveness); bronchitis; acute, allergic, atrophic rhinitis and chronic rhinitis including rhinitis caseosa, hypertrophic rhinitis, rhinitis purulenta, rhinitis sicca and rhinitis medicamentosa; membranous rhinitis including croupous, fibrinous and pseudomembranous rhinitis and scrofulous rhinitis; seasonal rhinitis including rhinitis nervosa (hay fever) and vasomotor rhinitis; sarcoidosis, farmer's lung and related diseases, fibroid lung and idiopathic interstitial pneumonia;
- (2) **(bone and joints)** rheumatoid arthritis, seronegative spondyloarthropathies (including ankylosing spondylitis, psoriatic arthritis and Reiter's disease), Behcet's disease, Sjogren's syndrome and systemic sclerosis;
- (3) **(skin)** psoriasis, atopic dermatitis, contact dermatitis and other eczmatous dermatides, seborrhoetic dermatitis, Lichen planus, Pemphigus, bullous Pemphigus, Epidermolysis bullosa, urticaria, angiodermas, vasculitides, erythemas, cutaneous eosinophilias, uveitis, Alopecia areata and vernal conjunctivitis;

(4) (**gastrointestinal tract**) Coeliac disease, proctitis, eosinophilic gastro-enteritis, mastocytosis, Crohn's disease, ulcerative colitis, food-related allergies which have effects remote from the gut, e.g., migraine, rhinitis and eczema;

5

(5) (**other tissues and systemic disease**) multiple sclerosis, atherosclerosis, Acquired Immunodeficiency Syndrome (AIDS), lupus erythematosus, systemic lupus, erythematosus, Hashimoto's thyroiditis, myasthenia gravis, type I diabetes, nephrotic syndrome, eosinophilia fascitis, hyper IgE syndrome, lepromatous leprosy, Sezary syndrome and idiopathic thrombocytopenia purpura;

10

(6) (**allograft rejection**) acute and chronic following, for example, transplantation of kidney, heart, liver, lung, bone marrow, skin and cornea; and chronic graft versus host disease;

15

(7) cancers, especially non-small cell lung cancer (NSCLC) and squamous sarcoma;

(8) diseases in which angiogenesis is associated with raised CXCR2 chemokine levels (e.g. NSCLC); and

20

(9) cystic fibrosis, stroke, re-perfusion injury in the heart, brain, peripheral limbs and sepsis.

25

Thus, the present invention provides a compound of formula (I), or a pharmaceutically-acceptable salt or solvate thereof, as hereinbefore defined for use in therapy.

In a further aspect, the present invention provides the use of a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as hereinbefore defined in the manufacture of a medicament for use in therapy.

30



In a still further aspect, the present invention provides the use of a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as hereinbefore defined in the manufacture of a medicament for the treatment of human diseases or conditions in which modulation of chemokine receptor activity is beneficial.

5

In the context of the present specification, the term "therapy" also includes "prophylaxis" unless there are specific indications to the contrary. The terms "therapeutic" and "therapeutically" should be construed accordingly.

10

The invention still further provides a method of treating a chemokine mediated disease wherein the chemokine binds to a CXCR2 receptor, which comprises administering to a patient a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as hereinbefore defined.

15

The invention also provides a method of treating an inflammatory disease, especially psoriasis, in a patient suffering from, or at risk of, said disease, which comprises administering to the patient a therapeutically effective amount of a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as hereinbefore defined.

20

For the above-mentioned therapeutic uses the dosage administered will, of course, vary with the compound employed, the mode of administration, the treatment desired and the disorder indicated.

25

The compounds of formula (I) and pharmaceutically acceptable salts and solvates thereof may be used on their own but will generally be administered in the form of a pharmaceutical composition in which the formula (I) compound/salt/solvate (active ingredient) is in association with a pharmaceutically acceptable adjuvant, diluent or carrier. Depending on the mode of administration, the pharmaceutical composition will preferably comprise from 0.05 to 99 %w (per cent by weight), more preferably from 0.05 to 80 %w,

still more preferably from 0.10 to 70 %w, and even more preferably from 0.10 to 50 %w, of active ingredient, all percentages by weight being based on total composition.

The present invention also provides a pharmaceutical composition comprising a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as hereinbefore defined, in association with a pharmaceutically acceptable adjuvant, diluent or carrier.

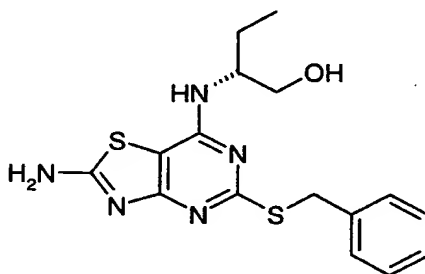
The invention further provides a process for the preparation of a pharmaceutical composition of the invention which comprises mixing a compound of formula (I), or a pharmaceutically acceptable salt or solvate thereof, as hereinbefore defined, with a pharmaceutically acceptable adjuvant, diluent or carrier.

The pharmaceutical compositions may be administered topically (e.g. to the lung and/or airways or to the skin) in the form of solutions, suspensions, heptafluoroalkane aerosols and dry powder formulations; or systemically, e.g. by oral administration in the form of tablets, capsules, syrups, powders or granules, or by parenteral administration in the form of solutions or suspensions, or by subcutaneous administration or by rectal administration in the form of suppositories or transdermally.

The invention will now be further illustrated by reference to the following examples. In the examples the Nuclear Magnetic Resonance (NMR) spectra were measured on a Varian Unity Inova 300 or 400 MHz spectrometer and the Mass Spectrometry (MS) spectra measured on a Finnigan Mat SSQ7000 or Micromass Platform spectrometer. Where necessary, the reactions were performed under an inert atmosphere of either nitrogen or argon. Chromatography was generally performed using Matrex Silica 60<sup>®</sup> (35-70 micron) or Prolabo Silica gel 60<sup>®</sup> (35-70 micron) suitable for flash silica gel chromatography. High pressure liquid chromatography purification was performed using either a Waters Micromass LCZ with a Waters 600 pump controller, Waters 2487 detector and Gilson FC024 fraction collector or a Waters Delta Prep 4000. The abbreviations m.p. and DMSO used in the examples stand for melting point and dimethyl sulphoxide respectively.

**Example 1**

**(2*R*)-2-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol**



**(a) 7-Chloro-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-amine**

2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one (0.89g) (prepared as described in Example 9), phosphorus oxychloride (12mL) and *N,N*-dimethylaniline (1.2mL) were heated at reflux for 2 hours. The cooled reaction mixture was poured onto ice and water and stirred for 2 hours. Chromatography on silica eluting with methanol/dichloromethane mixtures gave the sub-title chloride.

m.p. 217-218.5°C

MS: APCI(+ve) 309/11 (M+1)

<sup>1</sup>H NMR: δ (DMSO) 4.38 (s,2H), 7.20-7.48 (m,5H) and 8.95 (br s,2H).

**(b) (2*R*)-2-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol**

The chloro compound from step (a) (0.12g) in tetrahydrofuran (3 mL) was treated with (*R*)-2-amino-1-butanol (0.56g) and the reaction mixture was heated at reflux for 5 days. Dichloromethane and dilute hydrochloric acid were added. The resulting solid was filtered off, washed with water and ether to give the title compound which was obtained containing 0.23 moles of hydrogen chloride and 0.93 moles of water. Yield 0.045g.

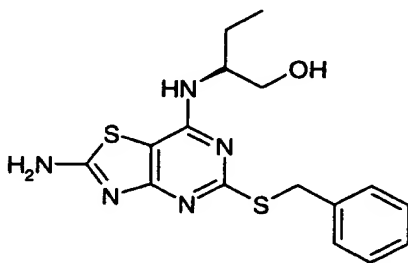
m.p. 118-121°C

MS: APCI(+ve) 362 (M+1)

<sup>1</sup>H NMR:  $\delta$  (DMSO) 0.83 (t,3H), 1.45 (m,2H), 1.65 (m,2H), 3.39 (m,2H), 4.31 (q,2H), 4.65 (t,1H), 6.91 (d,1H), 7.17-7.44 (m,5H) and 8.00 (s,2H).

## 5 Example 2

(*S*)-2-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol



Prepared by the method of Example 1(b) from the chloro compound of Example 1(a) and  
10 (*S*)-2-amino-1-butanol. Obtained as a solid containing 0.7 moles of hydrogen chloride.

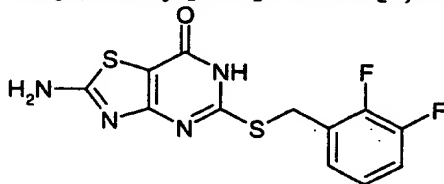
mp 204-208°C

MS: APCI(+ve) 362 (M+1)

<sup>1</sup>H NMR:  $\delta$  (DMSO) 0.82 (t,3H), 1.37-1.74 (m,2H), 3.36-3.52 (m,2H), 4.10 (br s,1H),  
15 4.41 (q,2H), 7.20-7.46 (m,5H), 7.63 (br s,1H) and 8.42 (s,2H).

## Example 3

2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one



20 a) 2-Amino-5-mercapto-thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one

Aluminium tribromide (1M in CH<sub>2</sub>Br<sub>2</sub>, 15.2ml) was added to a solution of the product of Example 9 (2.0g) in toluene (25ml) and the reaction mixture heated at 60°C for 6 hours.

On cooling to room temperature, water (40ml) was added and the resulting solid isolated by filtration then triturated with hot ethanol to afford the sub-title compound (0.8g).

MS: (APCI) 201 ( $M+H^+$ , 100%)

5

**b) 2-Amino-5-[[2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

Potassium *t*-butoxide solution (0.45mL of 1M in tetrahydrofuran) was added to a stirred solution of the product of step a) (0.09g) and 2,3-difluorobenzyl bromide in dimethyl sulphoxide (2mL). After stirring for 3 days, the reaction mixture was poured onto water.

10 The title compound was obtained. Yield 0.065g.

m.p. 310-313°C

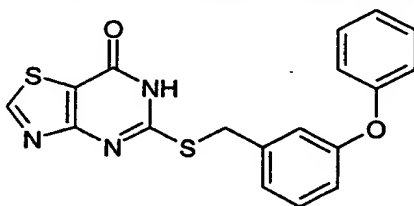
MS: APCI(+ve) 327 ( $M+1$ )

$^1H$  NMR:  $\delta$  (DMSO) 4.48 (s,2H), 7.18-7.45 (m,3H), 8.20 (s,2H) and 12.62 (s,1H).

15

**Example 4**

**5-[[3-Phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

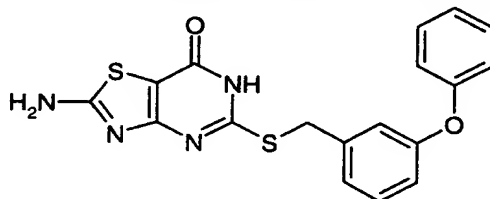


20 2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one (0.3g) (product of Example 5) was added over 90 minutes to a solution of *t*-butyl nitrite (0.17mL) in tetrahydrofuran (3mL) at 65°C. After a further 3.5 hours at 65°C, the solvent was evaporated and the residue chromatographed on silica eluting with methanol/dichloromethane mixtures to give the title compound. Yield 0.071g.

25 m.p. 197-198°C

MS: APCI(+ve) 368 ( $M+1$ )

$^1H$  NMR:  $\delta$  (DMSO) 4.49 (s,2H), 6.86-7.38 (m,9H), 9.58 (s,1H) and 13.11 (s,1H).

**Example 5****2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

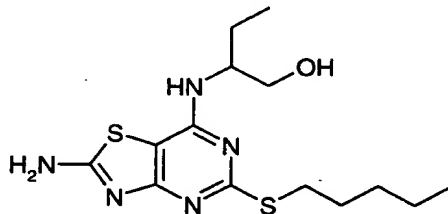
5 Prepared by the method of Example 3 using 3-phenoxybenzyl chloride.

m.p. 266-269°C

MS: APCI(+ve) 383 (M+1)

<sup>1</sup>H NMR: δ (DMSO) 4.40 (s,2H), 6.81-7.41 (m,9H), 8.15 (s,2H) and 12.55 (s,1H).

10

**Example 6****(±)-2-[[2-Amino-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol****(a) 7-Chloro-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-2-amine**

15 Prepared by the method of Example 1(a) from 2-amino-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one (product of Example 10).

m.p. 176.5-177.5°C

MS: APCI(+ve) 289 (M+1)

20 <sup>1</sup>H NMR: δ (DMSO) 0.88 (t,3H), 1.22-1.42 (m,4H), 1.60-1.74 (m,2H), 3.08 (t,2H) and 8.90 (s,2H).

**(b) (±)-2-[[2-Amino-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol**

Prepared by the method of Example 1(b) from the chloro compound of Example 6(a) and the appropriate amine.

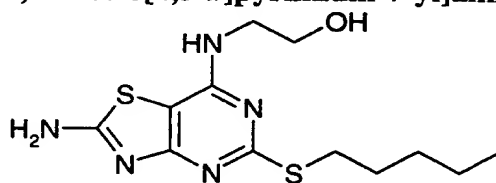
m.p. 151-154°C

5 MS: APCI(+ve) 342 (M+1)

<sup>1</sup>H NMR: δ (DMSO) 0.82-0.95 (m,6H), 1.22-1.72 (m,8H), 3.04 (m,2H), 3.39-3.56 (m,2H), 4.07 (m,1H), 4.64 (t,1H), 6.88 (d,1H), 7.44 (br s,1H) and 7.96 (s,2H).

### Example 7

10 2-[[2-Amino-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7-yl]amino]ethanol



Prepared by the method of Example 6(b).

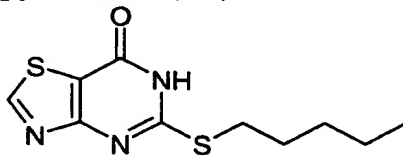
m.p. 192-195°C

15 MS: APCI(+ve) 314 (M+1)

<sup>1</sup>H NMR: δ (DMSO) 0.87 (t,3H), 1.21-1.42 (m,4H), 1.57-1.70 (m,2H), 2.99 (t,2H), 3.37-3.46 (m,2H), 3.46-3.58 (m,2H), 4.71 (t,1H), 7.22 (t,1H) and 7.97 (s,2H).

### Example 8

20 5-(Pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one



Prepared by the method of Example 4.

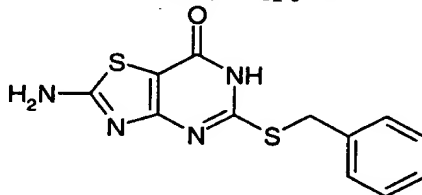
m.p. 208-209°C

25 MS: APCI(+ve) 256 (M+1)

<sup>1</sup>H NMR: δ (DMSO) 0.88 (t,3H), 1.22-1.44 (m,4H), 1.63-1.75 (m,2H), 3.20 (t,2H), 9.57 (s,1H) and 13.06 (s,1H).

### Example 9

#### 5 2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one



#### (a) 6-Amino-2-[(phenylmethyl)thio]-5-thiocyanato-4(1*H*)-pyrimidinone

6-Amino-2-[(phenylmethyl)thio]-4(1*H*)-pyrimidinone (10.5g) (prepared as described in WO 96/35678) and potassium thiocyanate (25g) in dimethylformamide (200mL) were  
10 heated together at 65°C. Pyridine (6.3mL) was added and the solution cooled to 5°C. Bromine (2.2mL) was added slowly and the reaction mixture stirred for 2 hours at 5-10°C. The reaction mixture was poured onto ice and water, stirred for 1 hour and the solid was filtered off. After washing with water and ether a pure sample was obtained after titration with hot methanol.

15

m.p. 260-262°C

MS: APCI(+ve) 291 (M+1)

<sup>1</sup>H NMR: δ (DMSO) 4.38 (s,2H), 7.21-7.51 (m,5H), 7.70 (br s,2H) and 12.35 (s,1H).

#### 20 (b) 2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one

The product of step (a) (7.35g) was heated at 120°C in dimethylformamide (40mL) and water (10mL) for 10 hours. After cooling, the resulting solid was filtered off, washed with water, ether and ethyl acetate to give the title compound containing 0.4 moles of dimethylformamide.

25

m.p. ~325°

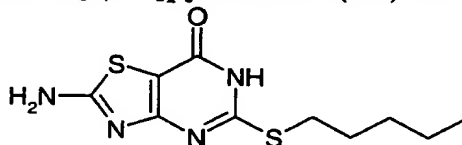
MS: APCI(+ve) 291 (M+1)



$^1\text{H}$  NMR:  $\delta$  (DMSO) 4.41 (s,2H), 7.21-7.50 (m,5H), 8.17 (s,2H) and 12.53 (br s,1H).

### Example 10

#### 2-Amino-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one



#### (a) 6-Amino-2-(pentylthio)-5-thiocyanato-4(1*H*)-pyrimidinone

Prepared by the method of Example 9(a).

m.p. 260-262°C

MS: APCI(+ve) 214 (M+1)

$^1\text{H}$  NMR:  $\delta$  (DMSO) 0.86 (t,3H), 1.22-1.40 (m,4H), 1.56-1.68 (m,2H), 3.10 (t,2H), 7.58 (br s,2H) and 12.30 (s,1H).

#### (b) 2-Amino-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one

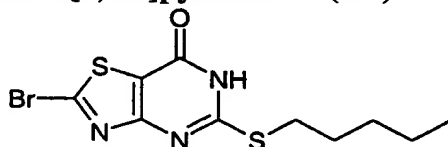
Prepared by the method of Example 9(b).

MS: APCI(+ve) 271 (M+1)

$^1\text{H}$  NMR:  $\delta$  (DMSO) 0.86 (t,3H), 1.24-1.40 (m,4H), 1.58-1.70 (m,2H), 3.12 (t,2H), 8.12 (br s,2H) and 12.49 (s,1H).

### Example 11

#### 2-Bromo-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one



Trimethylsilyl bromide (0.44mL) was added slowly to a solution at 0°C under nitrogen of t-butyl nitrite (0.42mL) in acetonitrile (2mL). After 30 minute at 0°C, 2-amino-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one (0.5g) (product of Example 10) was added.

The reaction mixture was stirred at room temperature for 16 hours and the solvent was evaporated. Chromatography on silica eluting with dichloromethane/methanol mixtures gave the title bromide.

5 m.p. 189-191°C

MS: APCI(+ve) 336/7 (M+1)

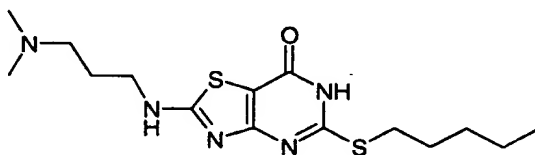
<sup>1</sup>H NMR: δ (DMSO) 0.88 (t,3H), 1.26-1.41 (m,4H), 1.64-1.75 (m,2H), 3.18 (t,2H) and 13.22 (s,1H).

## 10 Examples 12-26

The compounds of Examples 12 to 26 were prepared by heating 2-bromo-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one (product of Example 11) with 5 equivalents of the appropriate amine in tetrahydrofuran at 45°C for 5 hours.

## 15 Example 12

2-[[3-(Dimethylamino)propyl]amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one

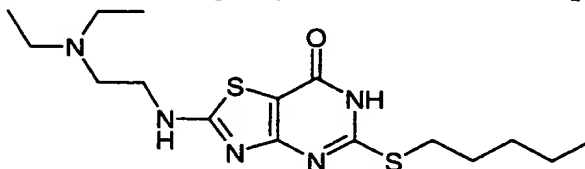


MS: APCI (+ve) 356 (M+1)

20

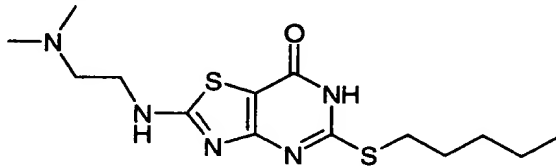
## Example 13

2-[[2-(Diethylamino)ethyl]amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one



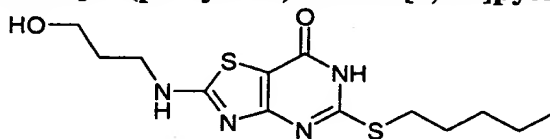
MS: APCI (+ve) 370 (M+1)

25

**Example 14****2-[[2-(Dimethylamino)ethyl]amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

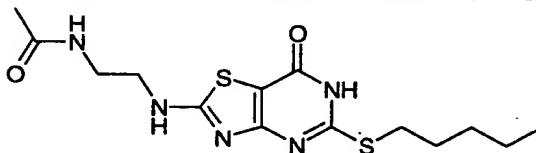
MS: APCI (+ve) 342 (M+1)

5

**Example 15****2-[(3-Hydroxypropyl)amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

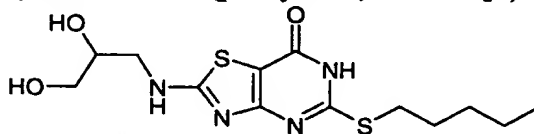
MS: APCI (+ve) 329 (M+1)

10

**Example 16****2-[[2-(Acetylamino)ethyl]amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

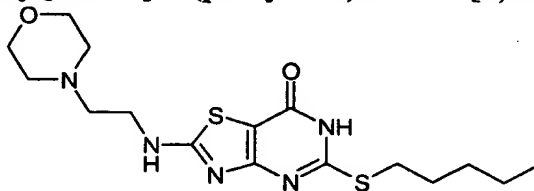
MS: APCI (+ve) 356 (M+1)

15

**Example 17****(±)-2-[(2,3-Dihydroxypropyl)amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

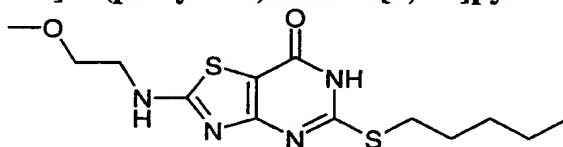
MS: APCI (+ve) 345 (M+1)

20

**Example 18****2-[[2-(4-Morpholinyl)ethyl]amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

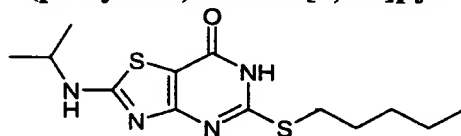
MS: APCI (+ve) 384 (M+1)

5

**Example 19****2-[(2-Methoxyethyl)amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

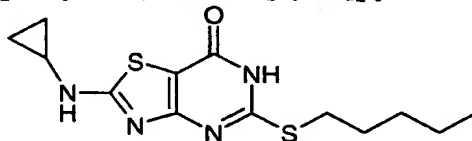
MS: APCI (+ve) 329 (M+1)

10

**Example 20****2-[(1-Methylethyl)amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

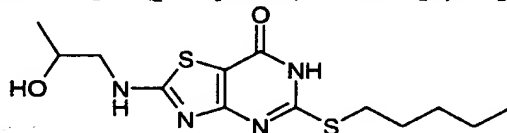
MS: APCI (+ve) 313 (M+1)

15

**Example 21****2-(Cyclopropylamino)-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

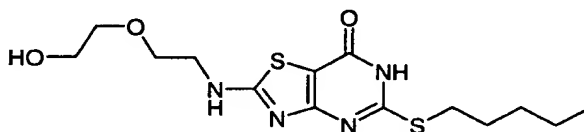
MS: APCI (+ve) 311 (M+1)

20

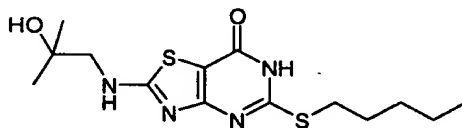
**Example 22****(±)-2-[(2-Hydroxypropyl)amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

MS: APCI (+ve) 329 (M+1)

5

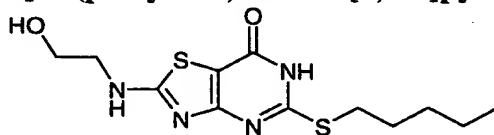
**Example 23****2-[[2-(2-Hydroxyethoxy)ethyl]amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

10 MS: APCI (+ve) 359 (M+1)

**Example 24****2-[(2-Hydroxy-2-methylpropyl)amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

15

MS: APCI (+ve) 343 (M+1)

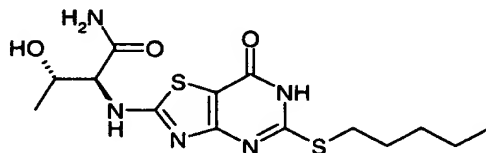
**Example 25****2-[(2-Hydroxyethyl)amino]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

20

MS: APCI (+ve) 315 (M+1)

**Example 26**

**(2*S*,3*R*)-3-Hydroxy-2-[(7-oxo-5-(pentylthio)-4*H*-thiazolo[4,5-*d*]pyrimidin-2-yl)-amino]butanamide**



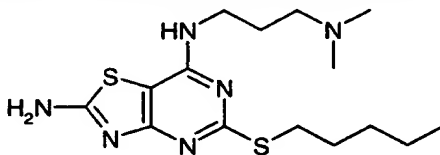
5 MS: APCI (+ve) 372 (M+1)

**Examples 27-43**

The compounds of Examples 27 to 43 were prepared by heating 7-chloro-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-2-amine (product of Example 6, step a) with 5  
10 equivalents of the appropriate amine in tetrahydrofuran at 45°C for 5 hours.

**Example 27**

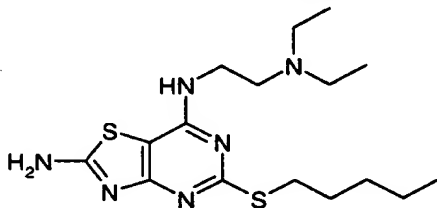
***N*<sup>7</sup>-[3-(Dimethylamino)propyl]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine**



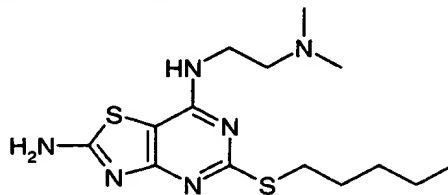
15 MS: APCI (+ve) 355 (M+1)

**Example 28**

***N*<sup>7</sup>-[2-(Diethylamino)ethyl]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine**

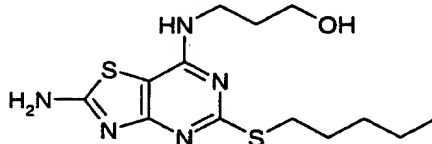


20 MS: APCI (+ve) 369 (M+1)

**Example 29*****N*<sup>7</sup>-[2-(Dimethylamino)ethyl]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine**

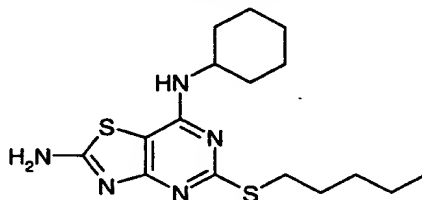
MS: APCI (+ve) 341 (M+1)

5

**Example 30****3-[(2-Amino-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-1-propanol**

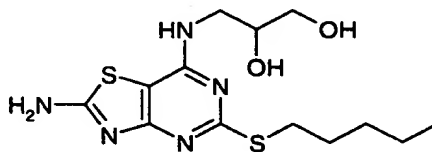
MS: APCI (+ve) 328 (M+1)

10

**Example 31*****N*<sup>7</sup>-Cyclohexyl-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine**

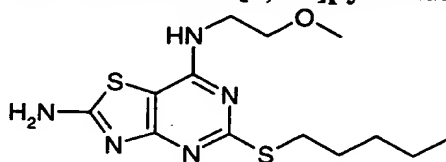
MS: APCI (+ve) 352 (M+1)

15

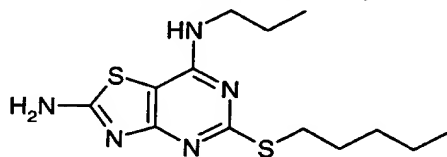
**Example 32****(±)-3-[(2-Amino-5-((phenylmethyl)thio)thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-1,2-propanediol**

20

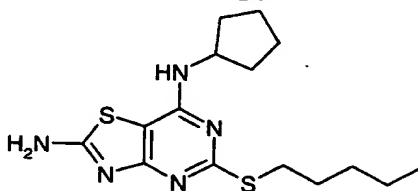
MS: APCI (+ve) 344 (M+1)

**Example 33*****N*<sup>7</sup>-(2-Methoxyethyl)-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine**

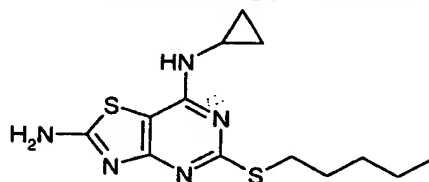
5 MS: APCI (+ve) 328 (M+1)

**Example 34****5-(Pentylthio)-*N*<sup>7</sup>-propylthiazolo[4,5-*d*]pyrimidine-2,7-diamine**

10 MS: APCI (+ve) 312 (M+1)

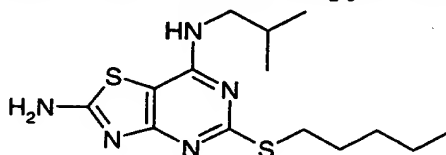
**Example 35*****N*<sup>7</sup>-Cyclopentyl-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine**

15 MS: APCI (+ve) 338 (M+1)

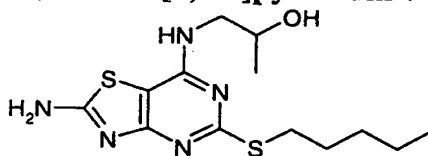
**Example 36*****N*<sup>7</sup>-Cyclopropyl-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine**

20 MS: APCI (+ve) 310 (M+1)

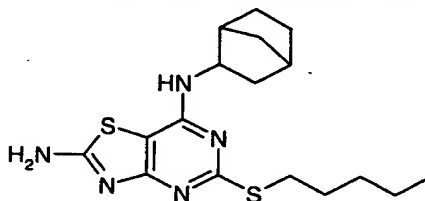


**Example 37*****N*<sup>7</sup>-(2-Methylpropyl)-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine**

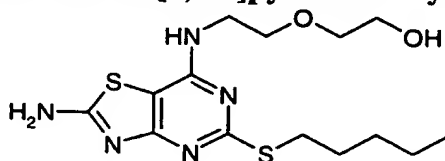
5 MS: APCI (+ve) 326 (M+1)

**Example 38****(±)-1-[(2-Amino-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7-yl)amino]-2-propanol**

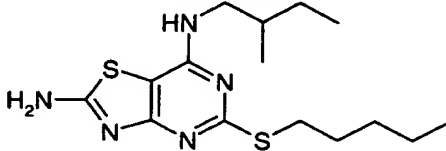
10 MS: APCI (+ve) 328 (M+1)

**Example 39****(exo)-*N*<sup>7</sup>-Bicyclo[2.2.1]hept-2-yl-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine**

15 MS: APCI (+ve) 364 (M+1)

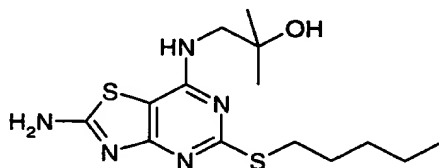
**Example 40****2-[2-[[2-Amino-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7-yl]amino]ethoxy]ethanol**

20 MS: APCI (+ve) 358 (M+1)

**Example 41****(±)-*N*<sup>7</sup>-(2-Methylbutyl)-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine**

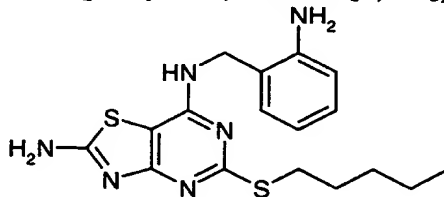
MS: APCI (+ve) 340 (M+1)

5

**Example 42****1-[[2-Amino-5-(pentylthio)thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-2-propanol**

MS: APCI (+ve) 342 (M+1)

10

**Example 43*****N*<sup>7</sup>-[(2-Aminophenyl)methyl]-5-(pentylthio)thiazolo[4,5-*d*]pyrimidine-2,7-diamine**

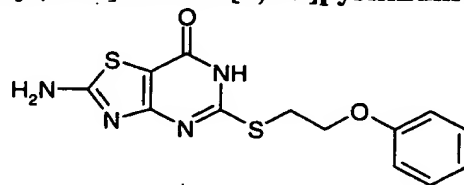
MS: APCI (+ve) 375 (M+1)

15

**Examples 44-47**

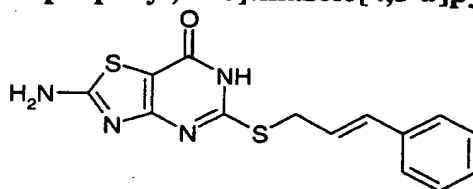
The compounds of Examples 44 to 47 were prepared from 2-amino-5,6-dihydro-5-thioxothiazolo[4,5-*d*]pyrimidin-7(4*H*)-one, diisopropylethylamine and the appropriate alkyl halide in dimethyl sulphoxide/dimethylformamide at 60°C. A total of 5 equivalents of base and alkyl halide were added over 3 days.

20

**Example 44****2-Amino-5-[(2-phenoxyethyl)thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

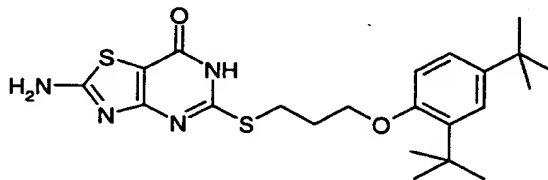
MS: APCI (+ve) 321 (M+1)

5

**Example 45****(*E*)-2-Amino-5-[(3-phenyl-2-propenyl)thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

MS: APCI (+ve) 317 (M+1)

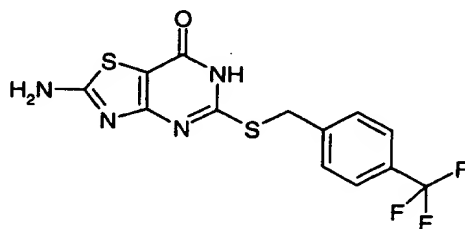
10

**Example 46****2-Amino-5-[[3-[2,4-bis(1,1-dimethylethyl)phenoxy]propyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

15 MS: APCI (+ve) 447 (M+1)

**Example 47**

**2-Amino-5-[[[(4-trifluoromethyl)phenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**



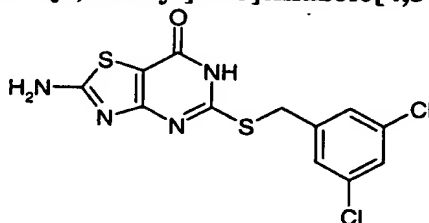
5 MS: APCI (+ve) 359 (M+1)

**Examples 48-65**

The compounds of Examples 48 to 65 were prepared from 2-amino-5,6-dihydro-5-thioxothiazolo[4,5-*d*]pyrimidin-7(4*H*)-one (product of Example 3, step a), potassium  
10 t-butoxide and the appropriate benzyl halide in dimethyl sulphoxide at room temperature. A total of 1.2 equivalents of base and alkyl halide were used and a reaction time of 24 hours.

**Example 48**

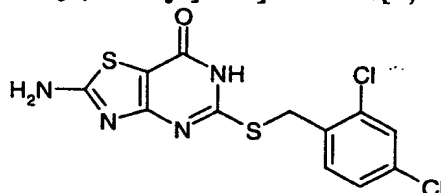
15 **2-Amino-5-[[[(3,5-dichlorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**



MS: APCI (+ve) 359 (M+1)

**Example 49**

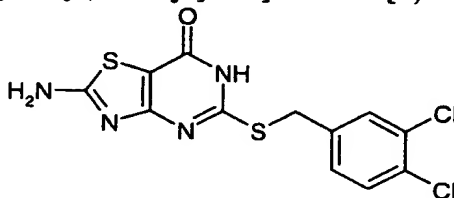
20 **2-Amino-5-[[[(2,4-dichlorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**



MS: APCI (+ve) 359 (M+1)

### Example 50

**2-Amino-5-[[[(3,4-dichlorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

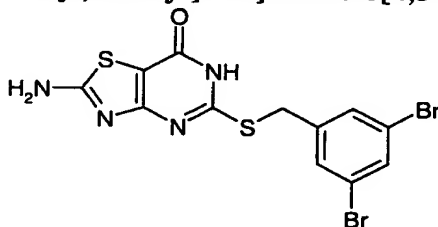


5

MS: APCI (+ve) 359 (M+1)

### Example 51

**2-Amino-5-[[[(3,5-dibromophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

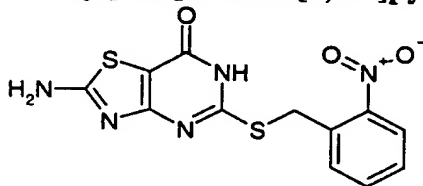


10

MS: APCI (+ve) 449 (M+1)

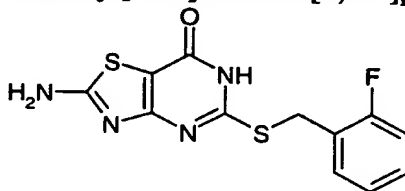
### Example 52

**2-Amino-5-[[[(2-nitrophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**



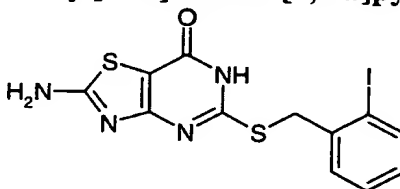
15

MS: APCI (+ve) 336 (M+1)

**Example 53****2-Amino-5-[[ (2-fluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

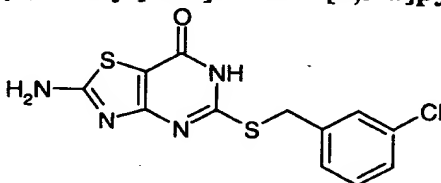
MS: APCI (+ve) 309 (M+1)

5

**Example 54****2-Amino-5-[[ (2-iodophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

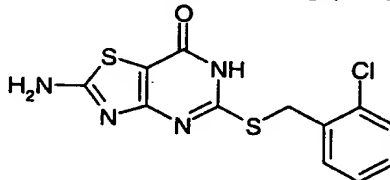
MS: APCI (+ve) 417 (M+1)

10

**Example 55****2-Amino-5-[[ (3-chlorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

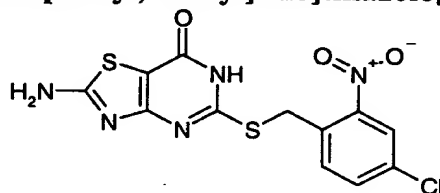
MS: APCI (+ve) 325 (M+1)

15

**Example 56****2-Amino-5-[[ (2-chlorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

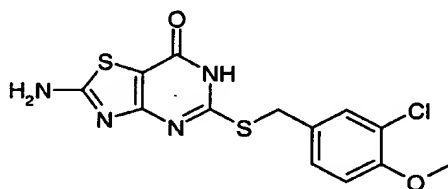
MS: APCI (+ve) 325 (M+1)

20

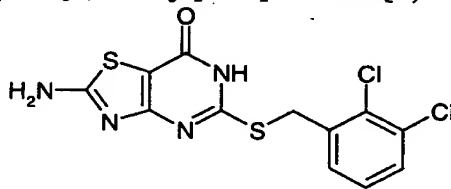
**Example 57****2-Amino-5-[[ (4-chloro-2-nitrophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

MS: APCI (+ve) 370 (M+1)

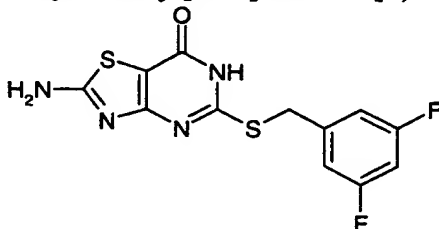
5

**Example 58****2-Amino-5-[[ (3-chloro-4-methoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

10 MS: APCI (+ve) 355 (M+1)

**Example 59****2-Amino-5-[[ (2,3-dichlorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

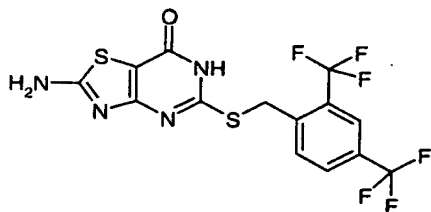
15 MS: APCI (+ve) 359 (M+1)

**Example 60****2-Amino-5-[[ (3,5-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

MS: APCI (+ve) 327 (M+1)

### Example 61

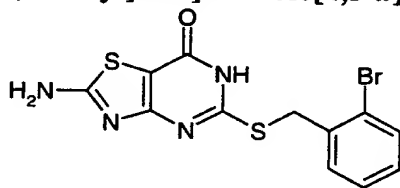
2-Amino-5-[[[(2,4-bis(trifluoromethyl)phenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one



MS: APCI (+ve) 427 (M+1)

### Example 62

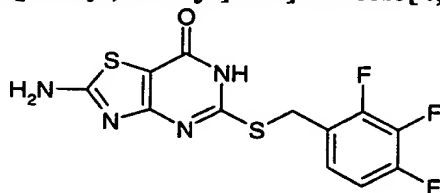
2-Amino-5-[[[(2-bromophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one



MS: APCI (+ve) 371 (M+1)

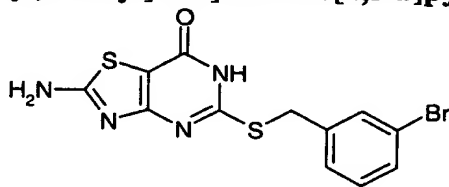
### Example 63

2-Amino-5-[[[(2,3,4-trifluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one



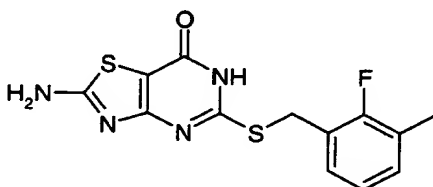
MS: APCI (+ve) 345 (M+1)



**Example 64****2-Amino-5-[[[(3-bromophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

MS: APCI (+ve) 369 (M+1)

5

**Example 65****2-Amino-5-[[[(2-fluoro-3-methylphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

10 MS: APCI (+ve) 323 (M+1)

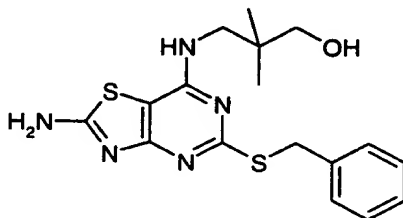
**Examples 66-77**

The compounds of Examples 66 to 77 were prepared from 7-chloro-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-amine and the appropriate hydroxyamine in dimethyl sulfoxide at 45°C. A total of 6 equivalents of amine were added and the reaction time was 2 days.

15

**Example 66****3-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2,2-dimethyl-1-propanol**

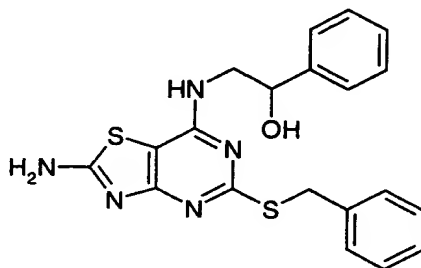
20



MS: APCI (+ve) 376 (M+1)

**Example 67**

(±)-α-[[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]methyl]benzenemethanol



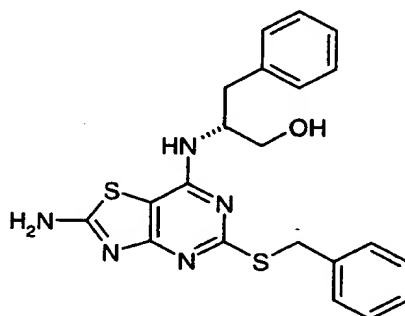
5

MS: APCI (+ve) 410 (M+1)

**Example 68**

(*R*)-β-[[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]benzenepropanol

10

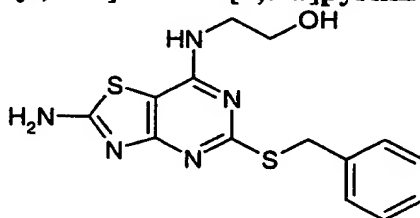


MS: APCI (+ve) 424 (M+1)

**Example 69**

2-[[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]ethanol

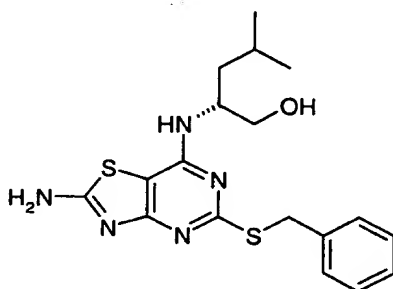
15



MS: APCI (+ve) 334 (M+1)

### Example 70

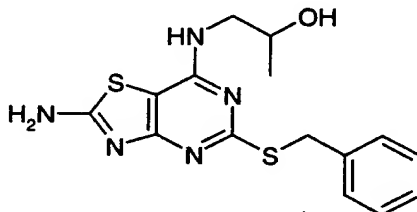
**(2*R*)-2-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]4-methylpentanol**



MS: APCI (+ve) 390 (M+1)

### Example 71

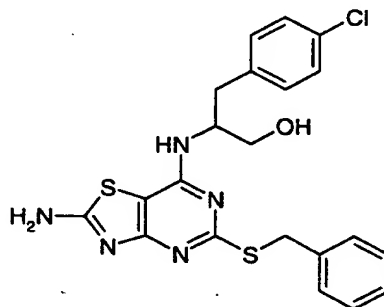
**(±)-1-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-propanol**



MS: APCI (+ve) 348 (M+1)

### Example 72

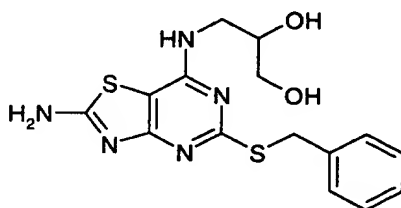
**(±)-β-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-4-chlorobenzenepropanol**



MS: APCI (+ve) 458 (M+1)

### Example 73

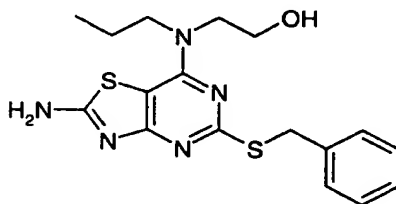
(±)-3-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1,2-propanediol



MS: APCI (+ve) 364 (M+1)

### Example 74

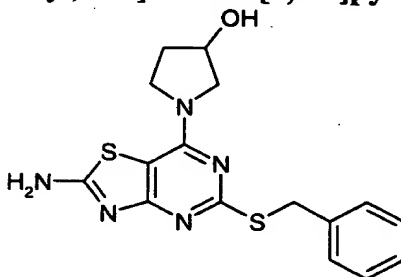
2-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-propylamino]ethanol



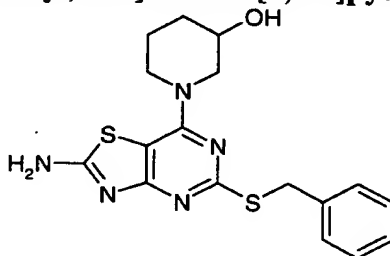
MS: APCI (+ve) 376 (M+1)

### Example 75

(±)-1-[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-3-pyrrolidinol

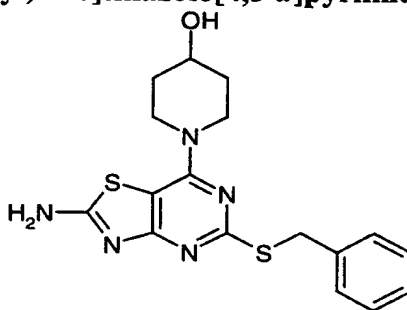


MS: APCI (+ve) 360 (M+1)

**Example 76****(±)-1-[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-3-piperidinol**

MS: APCI (+ve) 374 (M+1)

5

**Example 77****1-[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-4-piperidinol**

MS: APCI (+ve) 374 (M+1)

10

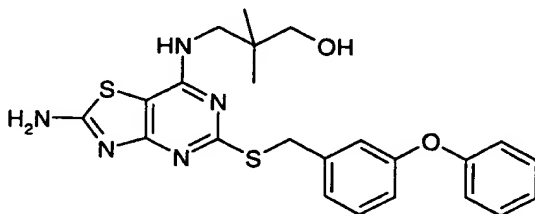
**Examples 78-110**

The compounds of Examples 78 to 110 were prepared from 7-chloro-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-2-amine (prepared by the method of Example 1, step a) using the product of Example 5) and the appropriate hydroxyamine in tetrahydrofuran at 45°C. A total of 6 equivalents of amine were added and the reaction time was 2 days.

15

**Example 78**

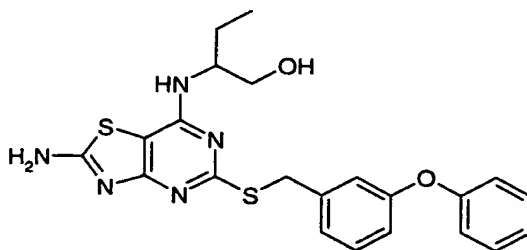
**3-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2,2-dimethyl-1-propanol**



5 MS: APCI (+ve) 468 (M+1)

**Example 79**

**(±)-2-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol**



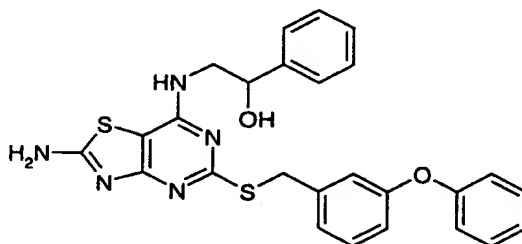
10

MS: APCI (+ve) 454 (M+1)

**Example 80**

**(±)-α-[[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]methyl]benzenemethanol**

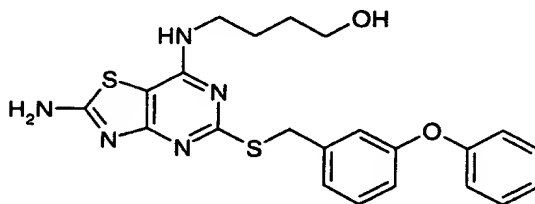
15



MS: APCI (+ve) 502 (M+1)

**Example 81**

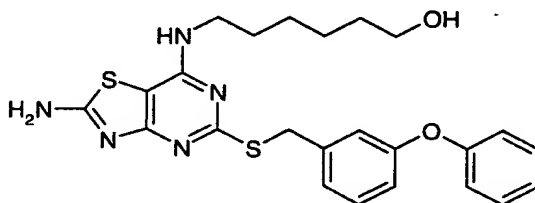
**4-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol**



5 MS: APCI (+ve) 454 (M+1)

**Example 82**

**6-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-hexanol**



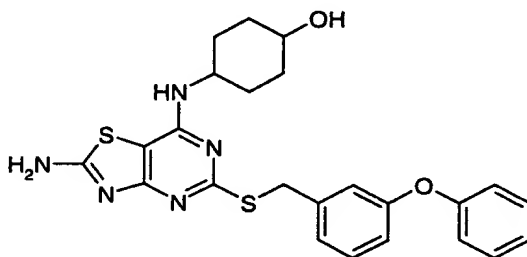
10

MS: APCI (+ve) 482 (M+1)

**Example 83**

**4-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-amino]cyclohexanol**

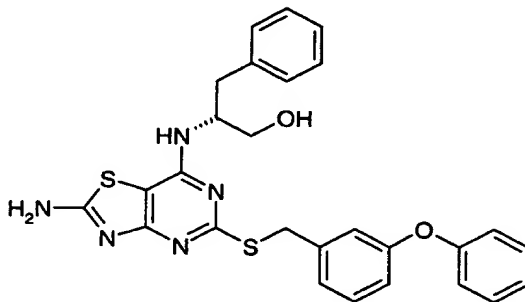
15



MS: APCI (+ve) 480 (M+1)

**Example 84**

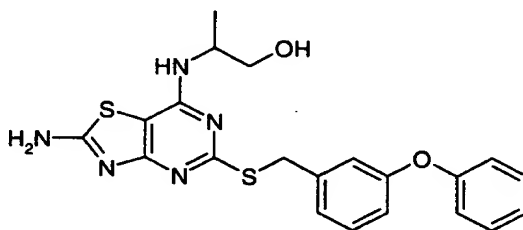
**(*R*)- $\beta$ -[[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-amino]benzenepropanol**



5 MS: APCI (+ve) 516 (M+1)

**Example 85**

**( $\pm$ )-2-[[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-amino]-1-propanol**



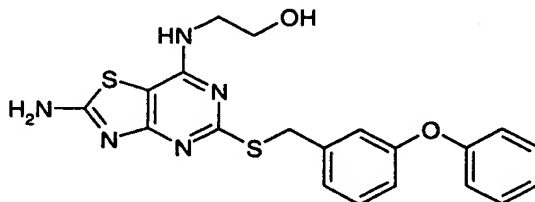
10

MS: APCI (+ve) 440 (M+1)

**Example 86**

**2-[[2-Amino-5-[[3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-amino]ethanol**

15

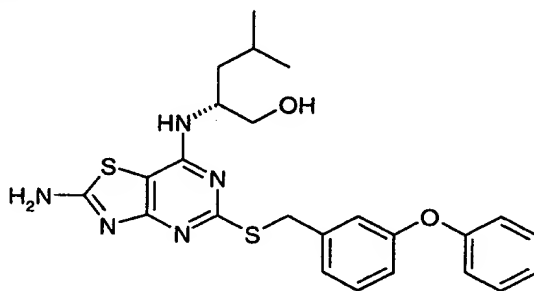


MS: APCI (+ve) 426 (M+1)



**Example 87**

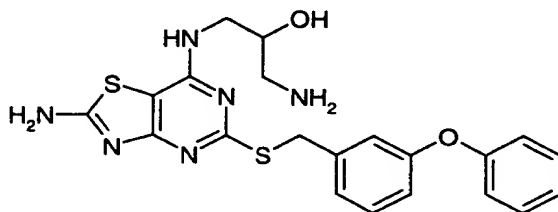
**(2*R*)-2-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-amino]-4-methylpentanol**



5 MS: APCI (+ve) 482 (M+1)

**Example 88**

**(±)-1-Amino-3-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-propanol**



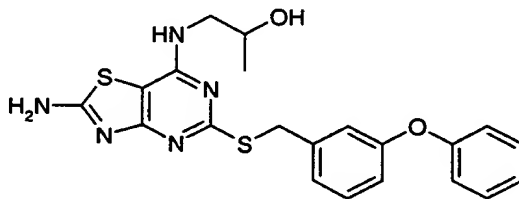
10

MS: APCI (+ve) 455 (M+1)

**Example 89**

**(±)-1-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-propanol**

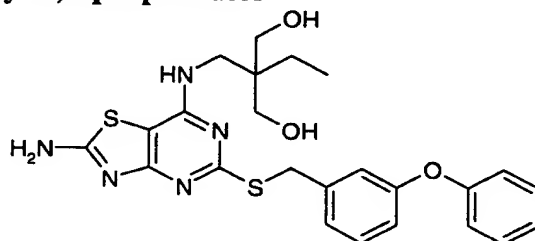
15



MS: APCI (+ve) 440 (M+1)

**Example 90**

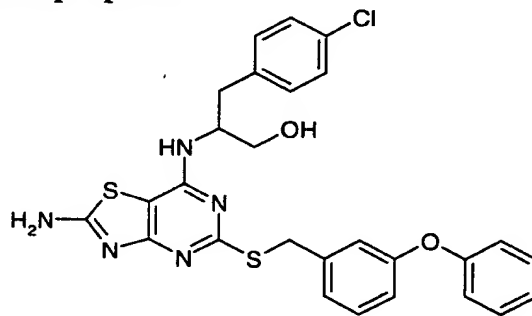
**2-[[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]methyl]-2-ethyl-1,3-propanediol**



5 MS: APCI (+ve) 498 (M+1)

**Example 91**

**(±)-β-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-4-chlorobenzenepropanol**



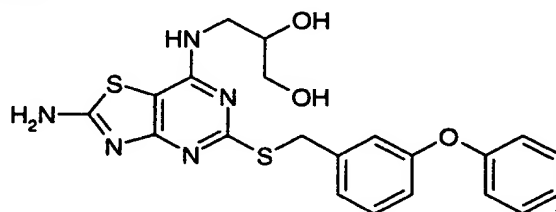
10

MS: APCI (+ve) 550 (M+1)

**Example 92**

**(±)-3-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1,2-propanediol**

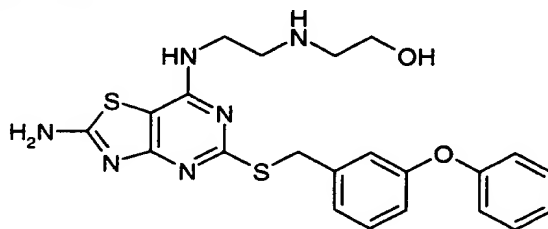
15



MS: APCI (+ve) 456 (M+1)

**Example 93**

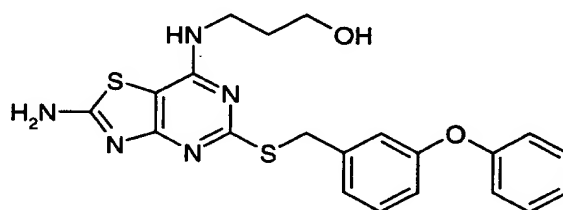
**2-[[2-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]ethyl]amino]ethanol**



5 MS: APCI (+ve) 469 (M+1)

**Example 94**

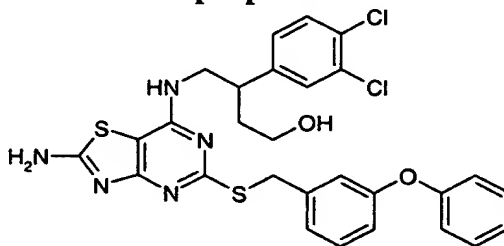
**3-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol**



10 MS: APCI (+ve) 440 (M+1)

**Example 95**

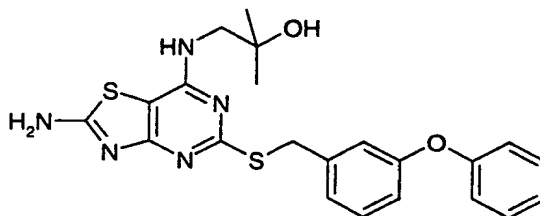
**(±)-α-[[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]methyl]-3,4-dichlorobenzenepropanol**



15 MS: APCI (+ve) 598 (M+1)

**Example 96**

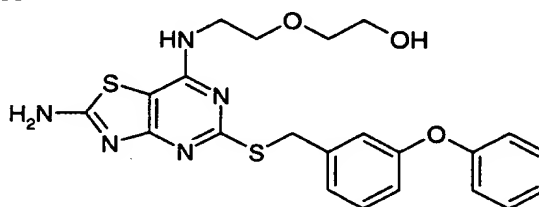
**1-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-2-propanol**



5 MS: APCI (+ve) 454 (M+1)

**Example 97**

**2-[2-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]ethoxy]ethanol**



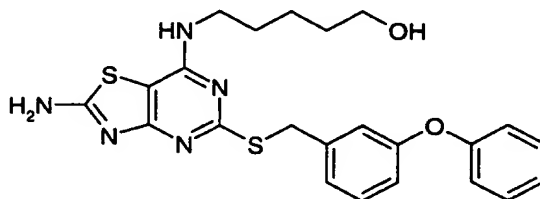
10

MS: APCI (+ve) 470 (M+1)

**Example 98**

**5-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-pentanol**

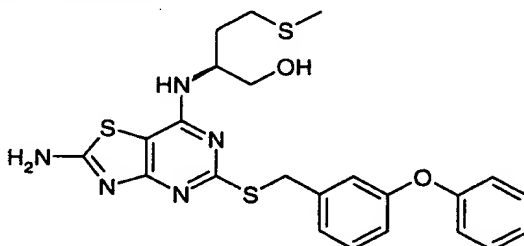
15



MS: APCI (+ve) 468 (M+1)

**Example 99**

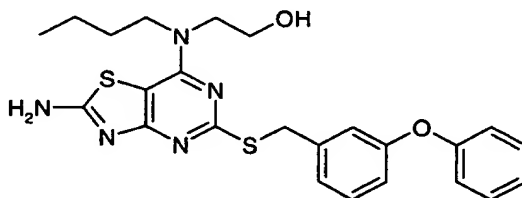
**(2*S*)-2-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-4-(methylthio)-1-butanol**



5 MS: APCI (+ve) 500 (M+1)

**Example 100**

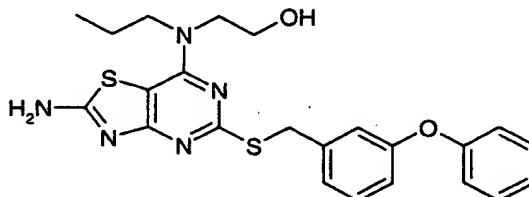
**2-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]butylamino]ethanol**



10 MS: APCI (+ve) 482 (M+1)

**Example 101**

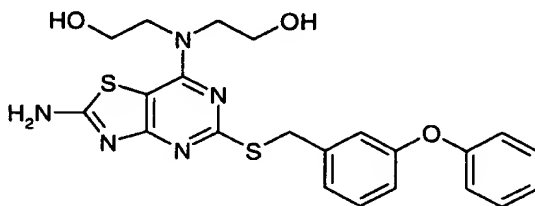
**2-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]propylamino]ethanol**



15 MS: APCI (+ve) 468 (M+1)

**Example 102**

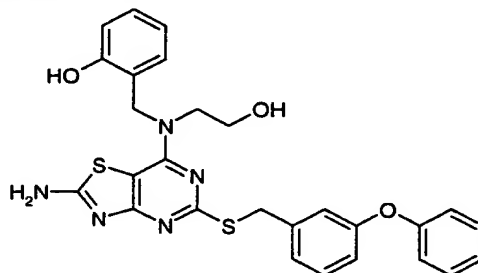
**2,2'-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]imino]bisethanol**



5 MS: APCI (+ve) 470 (M+1)

**Example 103**

**2-[[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-(2-hydroxyethyl)amino]methyl]phenol**



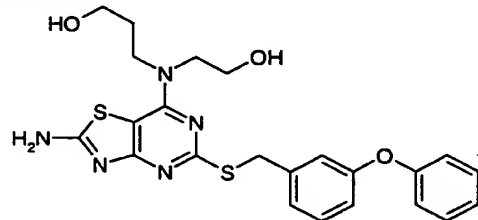
10

MS: APCI (+ve) 532 (M+1)

**Example 104**

**3-[[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-(2-hydroxyethyl)amino]-1-propanol**

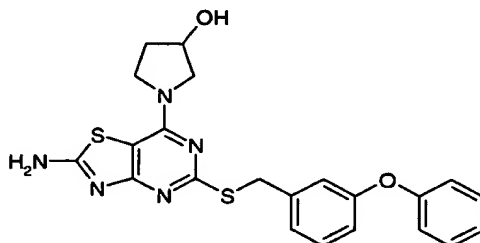
15



MS: APCI (+ve) 484 (M+1)

**Example 105**

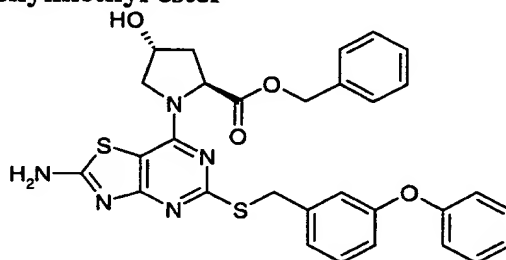
**(±)-1-[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-3-pyrrolidinol**



5 MS: APCI (+ve) 452 (M+1)

**Example 106**

**(*trans*)-1-[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-4-hydroxy-*L*-proline phenylmethyl ester**



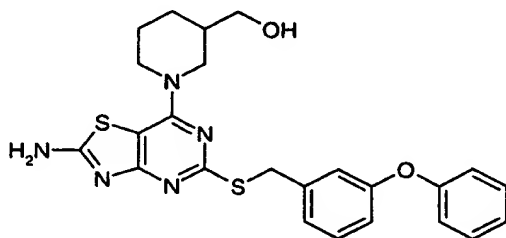
10

MS: APCI (+ve) 586 (M+1)

**Example 107**

**(±)-1-[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-3-piperidinemethanol**

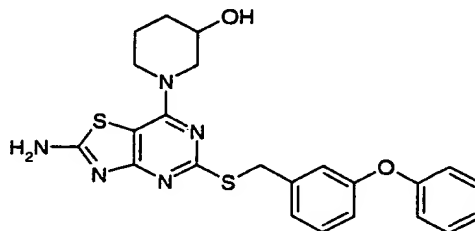
15



MS: APCI (+ve) 480 (M+1)

**Example 108**

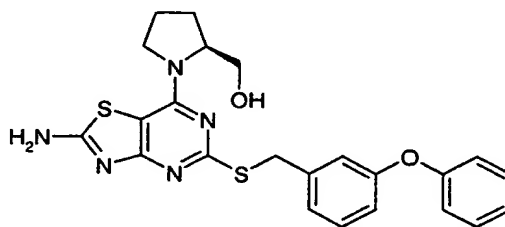
(±)-1-[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-3-piperidinol



5 MS: APCI (+ve) 466 (M+1)

**Example 109**

(2*S*)-1-[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-2-pyrrolidinemethanol



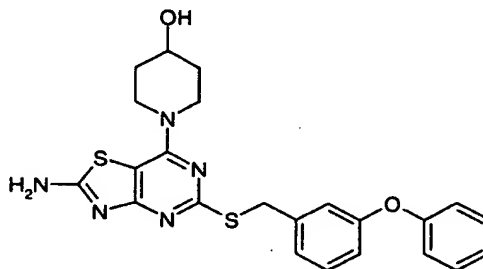
10

MS: APCI (+ve) 466 (M+1)

**Example 110**

1-[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-4-piperidinol

15

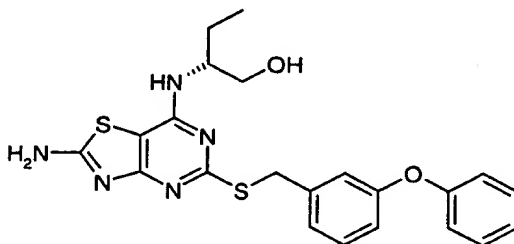


MS: APCI (+ve) 466 (M+1)



**Example 111**

**(2R)-2-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol**



- 5    **(a) 7-chloro-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-2-amine**  
Prepared by the method of Example 1(a).

m.p. 178-180°C

MS: APCI (+ve) 401 (M+1)

10    <sup>1</sup>H NMR: δ (DMSO) 4.37 (s, 2H), 6.83-7.39 (m, 9H) and 8.95 (s, 2H).

**(b) (2R)-2-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol**

Prepared by the method of Example 1(b).

15

m.p. 108-111°C

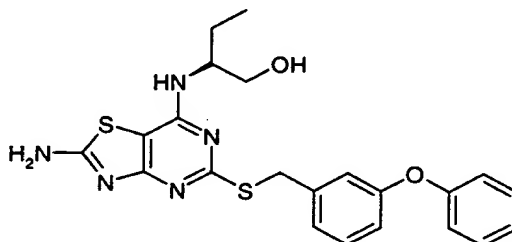
MS: APCI (+ve) 454 (M+1)

<sup>1</sup>H NMR: δ (DMSO) 0.81 (t, 3H), 1.41 (m, 2H), 1.62 (m, 2H), 3.36 (m, 2H), 4.03 (m, 1H),  
4.31 (q, 2H), 4.62 (s, 1H), 6.78-7.38 (m, 9H) and 8.00 (s, 2H).

20

**Example 112**

**(2S)-2-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-d]pyrimidin-7-yl]amino]-1-butanol**



5 Prepared by the method of Example 1(b).

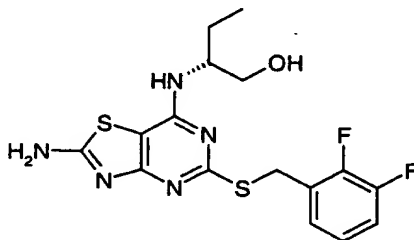
m.p. 111-114°C

MS: APCI (+ve) 454 (M+1)

<sup>1</sup>H NMR: δ (DMSO) 0.81 (t,3H), 1.41 (m,2H), 1.62 (m,2H), 3.36 (m,2H), 4.02 (br d,1H),  
 10 4.32 (q,2H), 4.60 (s,1H), 6.79-7.40 (m,9H) and 8.04 (s,2H).

**Example 113**

**(2R)-2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-d]pyrimidin-7-yl]amino]-1-butanol**



15

**(a) 7-Chloro-5-[[[(3,4-difluorophenyl)methyl]thio]thiazolo[4,5-d]pyrimidin-2-amine**

Prepared by the method of Example 1(a) using the product of Example 3.

m.p. 209-210°C

20 MS: APCI(+ve) 345/6 (M+1)

<sup>1</sup>H NMR: δ (DMSO) 4.45 (s,2H), 7.10-7.42 (m,3H) and 8.90 (br s,2H).

**(b) (2R)-2-[[2-Amino-5-[[[(3,4-difluorophenyl)methyl]thio]thiazolo[4,5-d]pyrimidin-7-yl]amino]-1-butanol**

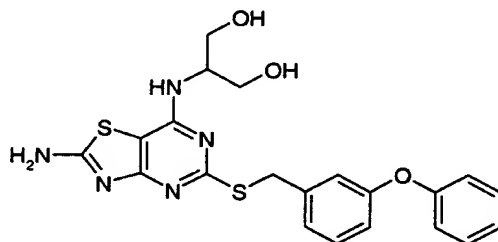
Prepared by the method of Example 1(b) using the product of step a) above.

MS: APCI(+ve) 398 (M+1)

$^1\text{H}$  NMR:  $\delta$  (DMSO) 0.82 (t,3H), 1.34-1.71 (m,4H), 3.37 (m,2H), 4.03 (br d,1H), 4.38 (q,2H), 4.62 (t,1H), 6.96 (d,1H), 7.06-7.40 (m,3H) and 8.02 (s,2H).

**Example 114**

**2-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-d]pyrimidin-7-yl]amino]-1,3-propanediol**



Prepared by the method of Example 1(b).

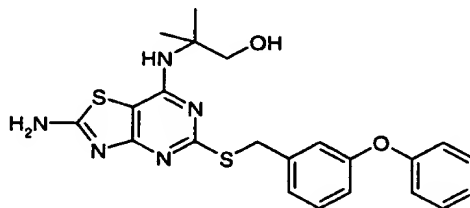
m.p. 220-222°C

MS: APCI (+ve) 456 (M+1)

$^1\text{H}$  NMR:  $\delta$  (DMSO) 3.50 (t,4H), 4.13 (m,1H), 4.32 (s,2H), 4.60 (t,2H), 6.78-7.40 (m,10H) and 8.01 (s,2H).

**Example 115**

**2-[[2-Amino-5-[[[(3-phenoxyphenyl)methyl]thio]thiazolo[4,5-d]pyrimidin-7-yl]amino]-2-methyl-1-propanol**



Prepared by the method of Example 1(b) with 10 equivalents of amine, 45-65°C and reaction time of 3 weeks. Purification by chromatography on silica eluting with methanol/dichloromethane mixtures gave the title compound.

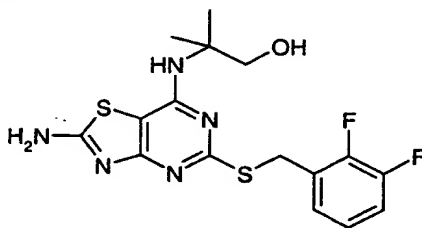
5 m.p. 126-130°C

MS: APCI (+ve) 454 (M+1)

<sup>1</sup>H NMR: δ (DMSO) 1.30 (s,6H), 3.53 (d,2H), 4.33 (s,2H), 4.86 (t,1H), 6.28 (s,1H), 6.80-7.40 (m,9H) and 8.00 (s,2H).

10 **Example 116**

**2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-d]pyrimidin-7-yl]amino]-2-methyl-1-propanol**



15 Prepared by the method of Example 1(b) using the product of Example 113, step a), 10 equivalents of amine, 45-65°C and reaction time of 3 weeks. Purification by chromatography on silica eluting with methanol/dichloromethane mixtures gave the title compound.

m.p. 231-234°C

20 MS: APCI (+ve) 398 (M+1)

<sup>1</sup>H NMR: δ (DMSO) 1.30 (s,6H), 3.53 (d,2H), 4.40 (s,2H), 4.84 (t,1H), 6.32 (s,1H), 7.10-7.40 (m,3H) and 8.03 (s,2H).

**Example 117****1-[[2-Amino-5-[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-2-propanol**

5 The product from Example 113, step a) (0.1g) and 1-amino-2-methyl-propan-2-ol (0.5g) in tetrahydrofuran (10ml) was heated in a sealed vessel at 100 °C for 18 hours. The mixture was evaporated to dryness and purified (HPLC, Novapak® C18 column, 0.1% aqueous ammonium acetate:acetonitrile, gradient elution 70:30 to 0:100 over 15 minutes) to afford the title compound (0.051g).

10 MS (APCI) 398 (M+H<sup>+</sup>, 100%).

NMR δH (d<sub>6</sub>-DMSO) 8.05 (2H, s), 7.39-7.17 (2H, m), 7.16-7.05 (2H, m), 4.51 (1H, s), 5.23 (1H, d), 4.39 (2H, s), 3.37 (2H, d), 1.06 (6H, s).

15 **Example 118**

**5-[(2,3-Difluorophenyl)methyl]thio]-*N*<sup>7</sup>-(2-fluoroethyl)thiazolo[4,5-*d*]pyrimidine-2,7-diamine**

20 The product from Example 113, step a) (0.1g), 2-fluoroethylamine hydrochloride (0.5g) and *N,N*-ethyldiisopropylamine (0.4ml) in tetrahydrofuran:water (7ml, 5:2) was heated in a sealed vessel at 100 °C for 18 hours. The mixture was evaporated to dryness and purified (HPLC, Novapak® C18 column, 0.1% aqueous ammonium acetate:acetonitrile, gradient elution 70:30 to 0:100 over 15 minutes) to afford the title compound (0.027g).

25 MS (APCI) 372 (M+H<sup>+</sup>, 100%).

NMR δH (d<sub>6</sub>-DMSO) 8.09 (2H, s), 7.36 (1H, t), 7.38-7.10 (3H, m), 4.57 (1H, t), 4.21 (3H,m), 3.71 (1H, q), 4.39 (2H, s), 3.63 (1H, q).

**Example 119**

**(1*R*-trans) 2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-cyclopentanol**

5 The product from example 113 step a) (0.2g), (1*R*,2*R*) 2-aminocyclopentanol hydrochloride (1.0g) and *N*-ethyldiisopropylamine (1.2ml) in methanol (15ml) was heated in a sealed vessel at 120 °C for 90 mins. The mixture was evaporated to dryness and purified (HPLC, Novapak® C18 column, 0.1% aqueous ammonium acetate:acetonitrile, gradient elution 70:30 to 0:100 over 15 minutes) to afford the title compound (0.098g).

10

MS (APCI) 410 (M+H<sup>+</sup>, 100%).

NMR δ<sub>H</sub> (d<sub>6</sub>-DMSO) 8.04 (2H, s), 7.41-7.27 (2H, m), 7.20 (1H, d), 7.16-7.11 (1H, m), 4.76 (1H, d), 4.41 (2H, dd), 4.09 (1H, m), 3.95 (1H, m), 1.99 (1H, m), 1.89 (1H, m), 1.62 (2H, m), 1.49-1.36 (2H, m).

15

**Example 120**

**(1*S*-trans) 2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-cyclopentanol**

20 Prepared by the method of Example 119 using the product from Example 113, step a) and (1*S*,2*S*)-2-aminocyclopentanol hydrochloride.

MS (APCI) 410 (M+H<sup>+</sup>, 100%).

25 NMR δ<sub>H</sub> (d<sub>6</sub>-DMSO) 8.03 (2H, s), 7.41-7.27 (2H, m), 7.20 (1H, d), 7.16-7.11 (1H, m), 4.76 (1H, d), 4.41 (2H, dd), 4.09 (1H, m), 3.96 (1H, m), 1.99 (1H, m), 1.89 (1H, m), 1.62 (2H, m), 1.49-1.36 (2H, m).

**Example 121****2-[[2-Amino-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol**

- 5 Prepared by the method of Example 117 using the product of Example 1, step a) (0.6g) and 2-amino-2-methyl-propanol. Purification (SiO<sub>2</sub>, ethyl acetate as eluant) gave the title compound (0.46g).

MS (APCI) 362 (M+H<sup>+</sup>, 100%).

- 10 NMR δH (d<sub>6</sub>-DMSO) 8.00 (2H, s), 7.42-7.20 (5H, m), 6.29 (1H, s), 4.86 (1H, s), 4.35 (2H, s), 3.56 (2H, d), 1.32 (6H, s).

**Example 122**

- 15 **2-Methyl-2-[[2-(methylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol**

**a) 2-[[2-Bromo-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol**

- 20 To a solution of the product from Example 121 (0.1g) in bromoform (5 ml) was added isoamyl nitrite (0.13 ml) and the mixture heated at 60°C for 10 mins. The mixture was evaporated to dryness then purified (SiO<sub>2</sub>, ethyl acetate: dichloromethane 1:9 as eluant) to give the subtitle compound (0.043g).

- 25 MS (APCI) 426 (M+H<sup>+</sup>, 100%).

**b) 2-Methyl-2-[[2-(methylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol**

To a solution of the product from step a) (0.043g) in methanol (5ml) was added a saturated solution of methanolic methylamine (20ml) and the mixture stirred for 30 mins. The mixture was evaporated to dryness and purified (HPLC, Novapak<sup>®</sup>C18 column, 0.1% aqueous ammonium acetate:acetonitrile, isocratic elution 70:30 over 15 minutes) to afford the title compound (0.026g).

MS (APCI) 376 (M+H<sup>+</sup>, 100%).

NMR  $\delta$ H (d<sub>6</sub>-DMSO) 8.49 (1H, d), 7.42-7.21 (5H, m), 6.34 (1H, s), 4.87 (1H, s), 4.35 (2H, s), 3.56 (2H, d), 2.94 (3H, d), 1.33 (6H, s).

### Example 123

**2-[[2-[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[(phenylmethyl)amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol**

**a) 2-[[2-Bromo-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol**

The sub-title compound was prepared by the method of Example 122, step a) using the product from Example 116. Purification (SiO<sub>2</sub>, ethyl acetate: dichloromethane 1:9 as eluant) gave the subtitle compound (0.16g).

MS (APCI) 461 (M+H<sup>+</sup>, 100%).

**b) 2-[[2-[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[(phenylmethyl)amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol**

Prepared by the method of Example 122, step b) using the product from step a).

Purification (SiO<sub>2</sub>, ethyl acetate: dichloromethane 1:9 as eluant) gave the title compound (0.051g).



MS (APCI) 488 (M+H<sup>+</sup>, 100%).

NMR  $\delta$ H (d<sub>6</sub>-DMSO) 9.08(1H, d), 7.38-7.12 (8H, m), 6.42 (1H, s), 4.82 (1H, t), 4.59 (2H, s), 4.42 (2H, s), 3.54 (2H, d), 1.29 (6H, s).

5 **Example 124**

**5-[[[(2,3-Difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

To a solution of the product from Example 3 (1.0g) in tetrahydrofuran (50ml) was added isoamyl nitrite (3ml) and the mixture heated at 70°C for 2 hours. The mixture was  
10 evaporated to dryness and purified (SiO<sub>2</sub>, ethyl acetate: chloroform 1:9 as eluant) to give the title compound (0.61g).

MS (APCI) 512 (M+H<sup>+</sup>, 100%).

NMR  $\delta$ H (d<sub>6</sub>-DMSO) 13.19(1H, s), 9.61(1H, d), 7.44-7.33 (2H, m), 7.22-15 (1H, m), 4.59  
15 (2H, s).

**Example 125-148**

Example 125 to 148 were prepared by heating, the product of Example 113, step a) (5x10<sup>-6</sup>  
20 moles) with the appropriate amine (10 equivalents) and *N*-ethyl-diisopropylamine (20 equivalents) in *N*-methylpyrrolidinone (0.3 ml) in a sealed vessel at 120°C for 16 hours.

**Example 125**

(±)-2-[[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-  
25 yl]amino]-1-butanol

MS (APCI) 398 (M+H<sup>+</sup>, 100%).

**Example 126**

**(1*S*,2*S*)-2-[[2-Amino-5-[[*(*2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-cyclohexanol**

5 MS (APCI) 424 (M+H<sup>+</sup>, 100%).

**Example 127**

**(±)-2-[[2-Amino-5-[[*(*2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol**

10

MS (APCI) 384 (M+H<sup>+</sup>, 100%)

**Example 128**

**2-[[2-Amino-5-[[*(*2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-ethanol**

15

MS (APCI) 370 (M+H<sup>+</sup>, 100%).

**Example 129**

**(2*R*)-2-[[2-Amino-5-[[*(*2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-4-methyl-1-pentanol**

20

MS (APCI) 426 (M+H<sup>+</sup>, 100%).

**Example 130**

**(±)-1-[[2-Amino-5-[[*(*2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-propanol**

25

MS (APCI) 384 (M+H<sup>+</sup>, 100%).

30

**Example 131**

**2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1,3-propanediol**

5 MS (APCI) 414 ( $M+H^+$ , 100%).

**Example 132**

**1-[[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]methyl]-cyclohexanol**

10

MS (APCI) 438 ( $M+H^+$ , 100%).

**Example 133**

**(2*R*)-2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol**

15

MS (APCI) 398 ( $M+H^+$ , 100%).

**Example 134**

**2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-(2-aminoethyl)amino]-1-ethanol**

20

MS (APCI) 413 ( $M+H^+$ , 100%).

25

**Example 135**

**2-[2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]ethoxy]-1-ethanol**

MS (APCI) 414 ( $M+H^+$ , 100%).

30

**Example 136**

**( $\alpha$ S)- $\alpha$ -[(1*R*)-1-[[2-Amino-5-[[2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]methylamino]ethyl]-benzenemethanol**

5 MS (APCI) 474 ( $M+H^+$ , 100%).

**Example 137**

**1-[2-Amino-5-[[2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-4-piperidinol**

10

MS (APCI) 410 ( $M+H^+$ , 100%).

**Example 138**

**5-[[2,3-Difluorophenyl)methyl]thio]-*N*<sup>7</sup>-ethyl-thiazolo[4,5-*d*]pyrimidine-2,7-diamine**

15

MS (APCI) 354 ( $M+H^+$ , 100%).

**Example 139**

**5-[[2,3-Difluorophenyl)methyl]thio]-*N*<sup>7</sup>-(2-propenyl)-thiazolo[4,5-*d*]pyrimidine-2,7-diamine**

20

MS (APCI) 366 ( $M+H^+$ , 100%).

**Example 140**

25 **2-Bromo-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

To a solution of the product from Example 9 (2g) in bromoform (100ml) was added isoamyl nitrite (2ml) and the mixture heated at 80°C for 2 hour. The mixture was evaporated to dryness and purified (SiO<sub>2</sub>, dichloromethane as eluant) to give the title compound (0.76g).

30

MS (APCI) 355, 354 (M+H<sup>+</sup>), 354 (100%).

**Example 141**

5 (1*S*,2*S*)-2-[[2-Amino-5-[[*(*2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-phenyl-1,3-propanediol

MS (APCI) 476 (M+H<sup>+</sup>, 100%).

10 **Example 142**

2-[[2-Amino-5-[[*(*2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1,3-propanediol

MS (APCI) 400 (M+H<sup>+</sup>, 100%).

15

**Example 143**

2-[[2-Amino-5-[[*(*2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-ethanol

20 MS (APCI) 370 (M+H<sup>+</sup>, 100%).

**Example 144**

(±)-5-[[*(*2,3-Difluorophenyl)methyl]thio]-*N*<sup>7</sup>-(2-methoxy-1-methylethyl)-thiazolo[4,5-*d*]pyrimidine-2,7-diamine

25

MS (APCI) 398 (M+H<sup>+</sup>, 100%).

**Example 145**

30 *N*<sup>7</sup>-Cyclopropyl-5-[[*(*2,3-difluorophenyl)methyl]thio]-thiazolo[4,5-*d*]pyrimidine-2,7-diamine

MS (APCI) 366 (M+H<sup>+</sup>, 100%).

**Example 146**

5 (±)-2-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]-thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol

MS (APCI) 384 (M+H<sup>+</sup>, 100%).

10 **Example 147**

4-[[2-Amino-5-[[[(2,3-difluorophenyl)methyl]thio]-thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol

MS (APCI) 398 (M+H<sup>+</sup>, 100%).

15

**Example 148**

5-[[[(2,3-Difluorophenyl)methyl]thio]-*N*<sup>7</sup>-[2-(1*H*-imidazol-4-yl)ethyl]-thiazolo[4,5-*d*]pyrimidine-2,7-diamine

20 MS (APCI) 420 (M+H<sup>+</sup>, 100%).

**Example 149-165**

The compounds of Example 149 to 165 were prepared by heating 2-[[2-bromo-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol  
25 (prepared according to the method of Example 122, step a) using the product of Example 116) (5×10<sup>-6</sup> moles) with the appropriate amine (2 equivalents) and *N*-ethyl-diisopropylamine (2 equivalents) in tetrahydrofuran (0.5 ml) at 50-60°C for 16 hours.

**Example 149**

***N*-[5-[[[(2,3-Difluorophenyl)methyl]thio]-7-[(2-hydroxy-1,1-dimethylethyl)amino]thiazolo[4,5-*d*]pyrimidin-2-yl]-serine, methyl ester**

5 MS (APCI) 500 ( $M+H^+$ , 100%).

**Example 150**

**2-[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[(1-methylethyl)amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol**

10 MS (APCI) 440 ( $M+H^+$ , 100%).

**Example 151**

**2-[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-(ethylamino)thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol**

15 MS (APCI) 426 ( $M+H^+$ , 100%).

**Example 152**

20 **2-[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[[2-(1*H*-indol-3-yl)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol**

MS (APCI) 541 ( $M+H^+$ , 100%).

**Example 153**

**2-[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[(1-naphthalenylmethyl)amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol**

30 MS (APCI) 538 ( $M+H^+$ , 100%).

**Example 154**

2-[[5-[(2,3-Difluorophenyl)methyl]thio]-2-[(1,2-diphenylethyl)amino]thiazolo[4,5-  
*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol

5

MS (APCI) 578 (M+H<sup>+</sup>, 100%).

**Example 155**

2-[[5-[(2,3-Difluorophenyl)methyl]thio]-2-[(2,2,2-trifluoroethyl)amino]thiazolo[4,5-  
*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol

10

MS (APCI) 480 (M+H<sup>+</sup>, 100%).

**Example 156**

2-[[5-[(2,3-Difluorophenyl)methyl]thio]-2-[(3,4,5-  
trimethoxyphenyl)methyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-  
propanol

15

MS (APCI) 578 (M+H<sup>+</sup>, 100%).

20

**Example 157**

2-[[5-[(2,3-Difluorophenyl)methyl]thio]-2-[(1,1-dimethylethyl)amino]thiazolo[4,5-  
*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol

25

MS (APCI) 454 (M+H<sup>+</sup>, 100%).

**Example 158**

2-[[5-[(2,3-Difluorophenyl)methyl]thio]-2-[[2-(2-thienyl)ethyl]amino]thiazolo[4,5-  
*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol

30



MS (APCI) 508 (M+H<sup>+</sup>, 100%).

**Example 159**

2-[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[(4-methylcyclohexyl)amino]thiazolo[4,5-  
5 *d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol

MS (APCI) 494 (M+H<sup>+</sup>, 100%).

**Example 160**

10 2-[[5-[[[(2,3-Difluorophenyl)methyl]thio]-7-[(2-hydroxy-1,1-  
dimethylethyl)amino]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-acetamide

MS (APCI) 455 (M+H<sup>+</sup>, 100%).

15 **Example 161**

2-[[2-[[2-(4-Aminophenyl)ethyl]amino]-5-[[[(2,3-  
difluorophenyl)methyl]thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-  
propanol

20 MS (APCI) 517 (M+H<sup>+</sup>, 100%).

**Example 162**

2-[[5-[[[(2,3-Difluorophenyl)methyl]thio]-2-[(2-fluoroethyl)amino]thiazolo[4,5-  
*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol

25 MS (APCI) 444 (M+H<sup>+</sup>, 100%).

**Example 163**

2-[[2-(Cyclopropylamino)-5-[[[(2,3-difluorophenyl)methyl]thio]thiazolo[4,5-  
30 *d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol

MS (APCI) 438 ( $M+H^+$ , 100%).

**Example 164**

5 **( $\pm$ )-2-[[5-[[2,3-Difluorophenyl)methyl]thio]-7-[(2-hydroxy-1,1-dimethylethyl)amino]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-1-pentanol**

MS (APCI) 484 ( $M+H^+$ , 100%).

10 **Example 165**

**2-[[5-[[2,3-Difluorophenyl)methyl]thio]-2-[[2-(2-hydroxyethoxy)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol**

15 MS (APCI) 486 ( $M+H^+$ , 100%).

**Example 166**

**2-Bromo-5-[[2,3-difluorophenyl)methyl]thio]-thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

20 To a solution of the product from Example 3 (0.2g) in bromoform (5ml) was added isoamyl nitrite (0.25ml) and the mixture heated at 70°C for 1 hour. The mixture was evaporated to dryness and purified ( $SiO_2$ , dichloromethane as eluant) to give the title compound (0.08g).

25 NMR  $\delta$ H ( $d_6$ -DMSO) 7.42-7.14 (3H, m), 4.55 (2H, s).

**Example 167-173**

The compounds of Example 167 to 173 were prepared by heating, the product of Example 166 with the appropriate amine (1.2 equivalents) and *N*-ethyldiisopropylamine (0.1 ml) in tetrahydrofuran (0.2 ml) at 40°C for 16 hours.

**Example 167**

*N*-[5-[[**(2,3-Difluorophenyl)methyl**]thio]-6,7-dihydro-7-oxo-thiazolo[4,5-*d*]pyrimidin-2-yl]-DL-serine, methyl ester

MS (APCI) 429 ( $M+H^+$ , 100%).

**Example 168**

5-[[**(2,3-Difluorophenyl)methyl**]thio]-2-[(1-methylethyl)amino]-thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one

MS (APCI) 369 ( $M+H^+$ , 100%).

**Example 169**

5-[[**(2,3-Difluorophenyl)methyl**]thio]-2-[[2-(1*H*-indol-3-yl)ethyl]amino]-thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one.

MS (APCI) 470 ( $M+H^+$ , 100%).

**Example 170**

2-[[5-[[**(2,3-Difluorophenyl)methyl**]thio]-6,7-dihydro-7-oxo-thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-acetamide

MS (APCI) 384 ( $M+H^+$ , 100%).

**Example 171**

**2-[[2-(4-Aminophenyl)ethyl]amino]-5-[[2,3-difluorophenyl)methyl]thio]-thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

5 MS (APCI) 446 (M+H<sup>+</sup>, 100%).

**Example 172**

**5-[[2,3-Difluorophenyl)methyl]thio]-2-[(2-fluoroethyl)amino]-thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

10

MS (APCI) 373 (M+H<sup>+</sup>, 100%).

**Example 173**

**5-[[2,3-Difluorophenyl)methyl]thio]-2-[[2-(2-hydroxyethoxy)ethyl]amino]-thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one**

15

MS (APCI) 415 (M+H<sup>+</sup>, 100%).

**Example 174-218**

20

Example 174 to 218 were prepared by heating the product of Example 122, step a) ( $5 \times 10^{-6}$  moles) with the appropriate amine (2 equivalents) and *N*-ethyldiisopropylamine (2 equivalents) in *N*-methylpyrrolidinone (0.1 ml) in a sealed vessel at 60°C for 5 hours.

**Example 174**

**2-[[2-(Cyclohexylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol**

MS (APCI) 444 (M+H<sup>+</sup>, 100%).

30

**Example 175**

**2-[[2-[(1,1-Dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol**

5 MS (APCI) 418 (M+H<sup>+</sup>, 100%).

**Example 176**

***N*-[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]-DL-alanine, methyl ester**

10

MS (APCI) 448 (M+H<sup>+</sup>, 100%).

**Example 177**

**4-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-cyclohexanol**

15

MS (APCI) 460 (M+H<sup>+</sup>, 100%).

**Example 178**

**2-Methyl-2-[[2-[(4-phenylbutyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol**

20

MS (APCI) 494 (M+H<sup>+</sup>, 100%).

**Example 179**

**2-Methyl-2-[[5-[(phenylmethyl)thio]-2-[[[(tetrahydro-2-furanyl)methyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol**

25

MS (APCI) 446 (M+H<sup>+</sup>, 100%).

30

**Example 180**

**2-Methyl-2-[[2-[(1-methylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol**

5 MS (APCI) 404 ( $M+H^+$ , 100%).

**Example 181**

**2-[[2-[[2-(4-Aminophenyl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol**

10 MS (APCI) 481 ( $M+H^+$ , 100%).

**Example 182**

***N*-[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]-L-valine, ethyl ester**

15 MS (APCI) 490 ( $M+H^+$ , 100%).

**Example 183**

20 **(2*S*)-2-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-4-methyl-pentanamide.**

MS (APCI) 475 ( $M+H^+$ , 100%).

**Example 184**

**2-Methyl-2-[[2-[(2-phenylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol**

30 MS (APCI) 466 ( $M+H^+$ , 100%).

**Example 185**

**2-[[2-[[4-Aminophenyl)methyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol**

5 MS (APCI) 467 (M+H<sup>+</sup>, 100%).

**Example 186**

**2-Methyl-2-[[5-[(phenylmethyl)thio]-2-[[2-(2-thienyl)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol**

10

MS (APCI) 472 (M+H<sup>+</sup>, 100%).

**Example 187**

**2-[[2-[(2-Fluoroethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol**

15

MS (APCI) 408 (M+H<sup>+</sup>, 100%).

**Example 188**

**2-Methyl-2-[[2-[[3-nitrophenyl)methyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol**

20

MS (APCI) 497 (M+H<sup>+</sup>, 100%).

**Example 189**

**( $\alpha R$ )- $\alpha$ -[(1*S*)-1-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-benzenemethanol**

MS (APCI) 496 (M+H<sup>+</sup>, 100%).

30

**Example 190**

**2-Methyl-2-[[5-[(phenylmethyl)thio]-2-[[[(3,4,5-trimethoxyphenyl)methyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol**

5 MS (APCI) 542 ( $M+H^+$ , 100%).

**Example 191**

**2-Methyl-2-[[2-[(1*R*-trans)-(2-phenylcyclopropyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol**

10 MS (APCI) 478 ( $M+H^+$ , 100%).

**Example 192**

**2-[[2-[[2-(1*H*-Indol-3-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol**

15

MS (APCI) 505 ( $M+H^+$ , 100%).

**Example 193**

**2-[[2-[(1,1-Dimethylpropyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol**

20

MS (APCI) 432 ( $M+H^+$ , 100%).

**Example 194**

**(±)-2-Methyl-2-[[2-[(1-methylbutyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol**

25

MS (APCI) 432 ( $M+H^+$ , 100%).

30



**Example 195**

(±)-2-Methyl-2-[[2-[(1-methylhexyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol

5 MS (APCI) 460 (M+H<sup>+</sup>, 100%).

**Example 196**

2-[[2-[[2-(2-Aminophenyl)methyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol

10 MS (APCI) 467 (M+H<sup>+</sup>, 100%).

**Example 197**

2-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-1,3-propanediol

15 MS (APCI) 436 (M+H<sup>+</sup>, 100%).

**Example 198**

20 2-[[2-[[2-(Ethylthio)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol

MS (APCI) 450 (M+H<sup>+</sup>, 100%).

**Example 199**

(2*S*)-2-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-3,3-dimethyl-1-butanol

25 MS (APCI) 462 (M+H<sup>+</sup>, 100%).

**Example 200**

( $\alpha S$ )- $\alpha$ -[(1*R*)-1-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-2-methoxyethyl]-benzenemethanol

5

MS (APCI) 526 ( $M+H^+$ , 100%).

**Example 201**

2-[[2-(Ethylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol

10

MS (APCI) 390 ( $M+H^+$ , 100%).

**Example 202**

2-[[2-[[[3-Fluoro-5-(trifluoromethyl)phenyl]methyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol

15

MS (APCI) 538 ( $M+H^+$ , 100%).

**Example 203**

( $\pm$ )-2-Methyl-2-[[2-[(1-methylpropyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol

20

MS (APCI) 418 ( $M+H^+$ , 100%).

25

**Example 204**

2-[[2-[[[4-Methoxyphenyl]methyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol

30

MS (APCI) 482 ( $M+H^+$ , 100%).

**Example 205**

2-[[2-[(2-Hydroxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol

5

MS (APCI) 406 (M+H<sup>+</sup>, 100%).

**Example 206**

2-[[2-[[2-(1*H*-Imidazol-4-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol

10

MS (APCI) 456 (M+H<sup>+</sup>, 100%).

**Example 207**

2-[[2-[(Diphenylmethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol

15

MS (APCI) 528 (M+H<sup>+</sup>, 100%).

**Example 208**

(2*S*)-2-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-1-butanol

20

MS (APCI) 434 (M+H<sup>+</sup>, 100%).

25

**Example 209**

2-[[2-[(2,2-Diethoxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol

30

MS (APCI) 478 (M+H<sup>+</sup>, 100%).

**Example 210**

4-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-1-butanol

5

MS (APCI) 434 ( $M+H^+$ , 100%).

**Example 211**

(1*S*,2*S*)-2-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-cyclohexanol.

10

MS (APCI) 460 ( $M+H^+$ , 100%).

**Example 212**

(±)-2-[[2-[(2-Hydroxy-1-methylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol

15

MS (APCI) 420 ( $M+H^+$ , 100%).

**Example 213**

2-[[2-[[2-(2-Hydroxyethoxy)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol

20

MS (APCI) 450 ( $M+H^+$ , 100%).

25

**Example 214**

(±)-2-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-1-pentanol

30 MS (APCI) 448 ( $M+H^+$ , 100%).

**Example 215**

**2-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-acetamide**

5

MS (APCI) 419 (M+H<sup>+</sup>, 100%).

**Example 216**

**(±)-2-[[2-[[1-(4-Fluorophenyl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-propanol**

10

MS (APCI) 484 (M+H<sup>+</sup>, 100%).

**Example 217**

**(1*R*,2*S*)-2-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-cyclohexanol**

15

MS (APCI) 460 (M+H<sup>+</sup>, 100%).

**Example 218**

**(α*S*)-α-[(1*R*)-1-[[7-[(2-Hydroxy-1,1-dimethylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-benzenemethanol**

20

MS (APCI) 496 (M+H<sup>+</sup>, 100%).

25

**Example 219**

**2-Bromo-7-chloro-5-[(phenylmethyl)thio]-thiazolo[4,5-*d*]pyrimidine**

To a solution of the product from Example 1, step a) (10g) in bromoform (300ml) was added *t*-butylnitrite (10ml) and the mixture heated at 60°C for 30 mins. The mixture was

30

evaporated to dryness then purified (SiO<sub>2</sub>, isohexane: dichloromethane 1:1 as eluant) to give the title compound (7.5g).

MS (APCI) 373 (M+H<sup>+</sup>, 100%).

5 NMR  $\delta$ H (d<sub>6</sub>-DMSO) 7.47-7.24 (5H, m), 4.49 (2H, s).

### Example 220

#### 7-Chloro-*N*-methyl-5-[(phenylmethyl)thio]-thiazolo[4,5-*d*]pyrimidin-2-amine

10 A solution of the product from Example 219 (0.3g) in tetrahydrofuran (2ml) containing methylamine (2.0 molar in THF:0.81ml) was stirred for 16 hours. The mixture was evaporated to dryness then purified (SiO<sub>2</sub>, ethyl acetate:dichloromethane 1:9 as eluant) to give the title compound (295mg).

15 MS (APCI) 323 (M+H<sup>+</sup>, 100%).

NMR  $\delta$ H (d<sub>6</sub>-DMSO) 9.30 (1H, s), 7.46-7.22 (5H, m), 4.40 (2H, s), 3.05 (3H, s).

### Example 221-223

20 Examples 221 to 223 were prepared by heating the product of Example 220 (2.5x10<sup>-6</sup> moles) with the appropriate amine (2 equivalents) and *N*-ethyldiisopropylamine (3 equivalents) in *N*-methylpyrrolidinone (0.1ml) in a sealed vessel at 100°C for 10 hours.

### Example 221

25 (±)-2-[[2-(Methylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol

MS (APCI) 362 (M+H<sup>+</sup>, 100%).

**Example 222**

**(2*R*)-4-Methyl-2-[[2-(methylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-pentanol**

5 MS (APCI) 404 ( $M+H^+$ , 100%).

**Example 223**

***N*-[2-(Methylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-L-serine, ethyl ester**

10

MS (APCI) 420 ( $M+H^+$ , 100%).

**Example 224**

**7-Chloro-5-[(phenylmethyl)thio]-*N*-[(tetrahydro-2-furanyl)methyl]-thiazolo[4,5-*d*]pyrimidin-2-amine**

15

Prepared according to the method of Example 220 using the product of Example 219 and tetrahydrofurfurylamine.

20 MS (APCI) 393 ( $M+H^+$ , 100%).

NMR  $\delta$ H ( $d_6$ -DMSO) 9.50 (1H, s), 7.47-7.19 (5H, m), 4.39 (2H, s), 4.06 (1H, m) 3.82 (1H, m), 3.66 (2H, m), 3.50 (1H, m), 2.00-1.53 (4H, m).

**Examples 225-228**

25

Examples 225-228 were prepared by the method of Example 221, using the product of Example 224.

**Examples 225**

(±)-2-[[5-[(Phenylmethyl)thio]-2-[[[(tetrahydro-2-furanyl)methyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol

5 MS (APCI) 446 (M+H<sup>+</sup>, 100%).

**Examples 226**

(±)-2-[[5-[(Phenylmethyl)thio]-2-[[[(tetrahydro-2-furanyl)methyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol

10

MS (APCI) 432 (M+H<sup>+</sup>, 100%).

**Examples 227**

(2*R*)-4-Methyl-2-[[5-[(phenylmethyl)thio]-2-[[[(tetrahydro-2-  
15 furanyl)methyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-pentanol

MS (APCI) 474 (M+H<sup>+</sup>, 100%).

**Examples 228**

20 *N*-[5-[(Phenylmethyl)thio]-2-[[[(tetrahydro-2-furanyl)methyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]-L-serine, ethyl ester

MS (APCI) 490 (M+H<sup>+</sup>, 100%).

**Example 229**

25 2-[2-[[7-Chloro-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethoxy]-1-ethanol

Prepared according to the method of Example 220 using the product of Example 219 (0.3g)  
30 and 2-(2-aminoethoxy)ethanol.



MS (APCI) 397 ( $M+H^+$ , 100%).

#### Example 230

5 (±)-2-[[2-[[2-(2-Hydroxyethoxy)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-  
d]pyrimidin-7-yl]amino]-1-propanol

Prepared by the method of Example 221, using the product of Example 229.

10 MS (APCI) 436 ( $M+H^+$ , 100%).

#### Example 231

4-[2-[[7-Chloro-5-[(phenylmethyl)thio]thiazolo[4,5-d]pyrimidin-2-yl]amino]ethyl]-  
benzenesulfonamide

15 A solution of the product from Example 219 (0.3g) in tetrahydrofuran (2ml) containing 4-  
(2-aminoethyl)benzenesulfonamide (0.161 g) and *N*-ethyldiisopropylamine (0.5 ml) was  
stirred for 16 hours. The mixture was evaporated to dryness then purified ( $SiO_2$ , ethyl  
acetate:dichloromethane 4:6 as eluant) to give the title compound (310mg).

20 MS (APCI) 492 ( $M+H^+$ , 100%).

NMR  $\delta$ H ( $d_6$ -DMSO) 9.45 (1H, s), 7.78-7.23 (9H, m), 4.41 (2H, s), 3.77 (2H, s) 3.02 (2H,  
t).

#### 25 Examples 232-235

Examples 232-235 were prepared by the method of Example 221, using the product of  
Example 231.

**Example 232**

(±)-4-[2-[[7-[[1-(Hydroxymethyl)propyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-benzenesulfonamide

5 MS (APCI) 545 (M+H<sup>+</sup>, 100%).

**Example 233**

(±)-4-[2-[[7-[(2-Hydroxy-1-methylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-benzenesulfonamide

10 MS (APCI) 531 (M+H<sup>+</sup>, 100%).

**Example 234**

4-[2-[[7-[(1*R*)-1-(Hydroxymethyl)-3-methylbutyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-benzenesulfonamide.

15 MS (APCI) 573 (M+H<sup>+</sup>, 100%).

**Example 235**

20 (±)-4-[2-[[7-[(2-Hydroxypropyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-benzenesulfonamide

MS (APCI) 531 (M+H<sup>+</sup>, 100%).

**Example 236**

7-Chloro-*N*-[2-(1*H*-imidazol-4-yl)ethyl]-5-[(phenylmethyl)thio]-thiazolo[4,5-*d*]pyrimidin-2-amine

Prepared according to the method of Example 231 using the product of Example 219 and  
30 histamine.

MS (APCI) 403 ( $M+H^+$ , 100%).

NMR  $\delta$ H ( $d_6$ -DMSO) 11.86 (1H, s), 9.42 (1H, s), 7.56 (1H, s), 7.56-7.23 (5H, m), 6.87 (1H, s), 4.41 (2H, s) 3.73 (2H, m), 2.85 (2H, t).

5

### Examples 237-248

Examples 237-248 were prepared by the method of Example 221, using the product of Example 236.

10

#### Example 237

*N*<sup>7</sup>-Ethyl-*N*<sup>2</sup>-[2-(1*H*-imidazol-4-yl)ethyl]-5-[(phenylmethyl)thiothiazolo[4,5-*d*]pyrimidine-2,7-diamine

15 MS (APCI) 412 ( $M+H^+$ , 100%).

#### Example 238

*N*<sup>2</sup>-[2-(1*H*-Imidazol-4-yl)ethyl]-5-[(phenylmethyl)thio]-*N*<sup>7</sup>-(3-pyridinylmethyl)-thiazolo[4,5-*d*]pyrimidine-2,7-diamine

20

MS (APCI) 475 ( $M+H^+$ , 100%).

#### Example 239

(±)-2-[[2-[[2-(1*H*-Imidazol-4-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol

25

MS (APCI) 456 ( $M+H^+$ , 100%).

**Example 240**

(±)-2-[[2-[[2-(1*H*-Imidazol-4-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol

5 MS (APCI) 442 (M+H<sup>+</sup>, 100%).

**Example 241**

(2*R*)-2-[[2-[[2-(1*H*-Imidazol-4-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-4-methyl-1-pentanol

10 MS (APCI) 484 (M+H<sup>+</sup>, 100%).

**Example 242**

(±)-1-[[2-[[2-(1*H*-Imidazol-4-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-propanol

15 MS (APCI) 442 (M+H<sup>+</sup>, 100%).

**Example 243**

20 5-[[2-[[2-(1*H*-Imidazol-4-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-pentanol

MS (APCI) 470 (M+H<sup>+</sup>, 100%).

**Example 244**

25 1-[2-[[2-(1*H*-Imidazol-4-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-4-(phenylmethyl)-4-piperidinol

MS (APCI) 558 (M+H<sup>+</sup>, 100%).

**Example 245**

(±)-1-[2-[[2-(1*H*-Imidazol-4-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-3-piperidinecarboxamide

5 MS (APCI) 495 (M+H<sup>+</sup>, 100%).

**Example 246**

2-[Ethyl[2-[[2-(1*H*-imidazol-4-yl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-ethanol

10

MS (APCI) 456 (M+H<sup>+</sup>, 100%).

**Example 247**

*N*<sup>2</sup>-[2-(1*H*-Imidazol-4-yl)ethyl]-*N*<sup>7</sup>,*N*<sup>7</sup>-dimethyl-5-[(phenylmethyl)thio]-thiazolo[4,5-*d*]pyrimidine-2,7-diamine

15

MS (APCI) 412 (M+H<sup>+</sup>, 100%).

**Example 248**

*N*<sup>7</sup>-[2-(Diethylamino)ethyl]-*N*<sup>7</sup>-ethyl-*N*<sup>2</sup>-[2-(1*H*-imidazol-4-yl)ethyl]-5-[(phenylmethyl)thio]-thiazolo[4,5-*d*]pyrimidine-2,7-diamine

20

MS (APCI) 511 (M+H<sup>+</sup>, 100%).

**Example 249**

7-Chloro-*N*-(2-phenoxyethyl)-5-[(phenylmethyl)thio]-thiazolo[4,5-*d*]pyrimidin-2-amine

25

Prepared by the method of Example 231, using the product of Example 219 and 2-phenoxyethylamine.

30

MS (APCI) 429 (M+H<sup>+</sup>, 100%).

NMR  $\delta$ H (d<sub>6</sub>-DMSO) 9.65 (1H, s), 7.46-6.93 (10H, m), 4.41 (2H, s), 4.20 (2H, t), 3.87 (2H, m).

5

### Examples 250-255

Examples 250-255 were prepared by the method of Example 221, using the product of Example 249.

10

#### Example 250

*N*<sup>2</sup>-(2-Phenoxyethyl)-5-[(phenylmethyl)thio]-*N*<sup>7</sup>-(3-pyridinylmethyl)-thiazolo[4,5-*d*]pyrimidine-2,7-diamine

15

MS (APCI) 501 (M+H<sup>+</sup>, 100%).

#### Example 251

*N*<sup>2</sup>-(2-Phenoxyethyl)-*N*<sup>7</sup>-[1-(phenylmethyl)-4-piperidinyl]-5-[(phenylmethyl)thio]-thiazolo[4,5-*d*]pyrimidine-2,7-diamine

20

MS (APCI) 583 (M+H<sup>+</sup>, 100%).

#### Example 252

2-Methyl-2-[[2-[(2-phenoxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol.

25

MS (APCI) 482 (M+H<sup>+</sup>, 100%).

**Example 253**

(±)-2-[[2-[(2-Phenoxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol

5 MS (APCI) 468 (M+H<sup>+</sup>, 100%).

**Example 254**

(2*R*)-4-Methyl-2-[[2-[(2-phenoxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-pentanol

10

MS (APCI) 510 (M+H<sup>+</sup>, 100%).

**Example 255**

1-[2-[(2-Phenoxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-4-(phenylmethyl)-4-piperidinol.

15

MS (APCI) 584 (M+H<sup>+</sup>, 100%).

**Example 256**

20 **7-Chloro-*N*-cyclopropyl-5-[(phenylmethyl)thio]-thiazolo[4,5-*d*]pyrimidin-2-amine,**

Prepared by the method of Example 220, using the product of Example 219 and cyclopropanamine.

25 MS (APCI) 351, 349 (M+H<sup>+</sup>, 100%).

NMR δH (d<sub>6</sub>-DMSO) 7.46-7.22 (5H, m), 4.41 (2H, s), 2.85-2.80 (1H, m), 0.90-0.84 (2H, m), 0.71-0.66 (2H, m).

**Examples 257-260**

Example 257 to 260 were prepared by the method of Example 221 using the product of Example 256.

5

**Example 257**

**2-[[2-(Cyclopropylamino)-5-[(phenylmethyl)thio]thiazolo [4,5-*d*]pyrimidin-7-yl]amino]-1-butanol**

10 MS (APCI) 402 (M+H<sup>+</sup>, 100%).

**Example 258**

**2-[[2-(Cyclopropylamino)-5-[(phenylmethyl)thio]thiazolo [4,5-*d*]pyrimidin-7-yl]amino]-1-propanol**

15

MS (APCI) 388 (M+H<sup>+</sup>, 100%).

**Example 259**

**(2*R*)-2-[[2-(Cyclopropylamino)-5-[(phenylmethyl)thio]thiazolo [4,5-*d*]pyrimidin-7-yl]amino]-4-methyl-1-pentanol**

20

MS (APCI) 430 (M+H<sup>+</sup>, 100%).

**Example 260**

***N*-[2-(Cyclopropylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-L-serine, ethyl ester**

25

MS (APCI) 446 (M+H<sup>+</sup>, 100%).



**Example 261****2-[[7-Chloro-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-1-pentanol**

Prepared by the method of Example 231, using the product of Example 219 and  
5 2-amino-1-pentanol.

MS (APCI) 397, 395 ( $M+H^+$ , 100%).

$^1H$  NMR ( $d_6$ -DMSO)  $\delta$  9.29 (1H, s), 7.46-7.22 (5H, m), 4.93 (1H, t), 4.39 (2H, s), 4.07-  
4.00 (1H, m), 3.50 (2H, t), 1.63-1.43 (2H, m), 1.38-1.32 (2H, m), 0.89 (3H, t).

**Examples 262-264**

Example 262 to 264 were prepared by the method of Example 221 using the product of  
Example 261.

**Example 262****(2*R*)-2-[[2-[[1-(Hydroxymethyl)butyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-4-methyl-1-pentanol**

MS (APCI) 476 ( $M+H^+$ , 100%).

**Example 263*****N*-[2-[[1-(Hydroxymethyl)butyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]-L-serine, ethyl ester**

MS (APCI) 492 ( $M+H^+$ , 100%).

**Example 264****( $\pm$ )-2-[[7-[Cyclohexyl(2-hydroxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-1-pentanol**

MS (APCI) 502 ( $M+H^+$ , 100%).

#### Examples 265-270

- 5 The following examples were prepared by the method of Example 221, using the product of Example 229.

#### Examples 265

- 10 **2-[2-[[7-(Ethylamino)-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethoxy]-1-ethanol**

MS (APCI) 406 ( $M+H^+$ , 100%).

#### Examples 266

- 15 **2-[2-[[7-[(1-Methylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethoxy]-1-ethanol**

MS (APCI) 420 ( $M+H^+$ , 100%).

#### 20 Examples 267

- (±)-2-[[2-[[2-(2-Hydroxyethoxy)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol,**

MS (APCI) 450 ( $M+H^+$ , 100%).

25

#### Examples 268

- 2-[[2-[[2-(2-Hydroxyethoxy)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-methyl-1-propanol**

- 30 MS (APCI) 450 ( $M+H^+$ , 100%).

**Examples 269**

(2*R*)-2-[[2-[[2-(2-Hydroxyethoxy)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-4-methyl-1-pentanol,

MS (APCI) 478 (M+H<sup>+</sup>, 100%).

**Examples 270**

2-[Cyclohexyl-[2-[[2-(2-hydroxyethoxy)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-ethanol

MS (APCI) 504 (M+H<sup>+</sup>, 100%).

**Examples 271**

(±)-2-[[5-[(Phenylmethyl)thio]-2-(4-piperidinylamino)thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol

**a) 7-Chloro-5-[(phenylmethyl)thio]-*N*-(4-piperidinyl)-thiazolo[4,5-*d*]pyrimidin-2-amine**

A solution of the product from Example 219 (0.3g) in tetrahydrofuran (2ml) containing 4-amino-1-piperidinecarboxylic acid, 1,1-dimethylethyl ester (0.161g) and *N*-ethyldiisopropylamine (0.5 ml) was stirred for 16 hours before evaporating to dryness. The residue was taken into dichloromethane (30ml) and trifluoroacetic acid (3ml) added. The solution was stirred for 30 minutes then concentrated to give the title compound (310mg).

MS (APCI) 392 (M+H<sup>+</sup>, 100%).

NMR δH (d<sub>6</sub>-DMSO) 9.47 (1H, s), 8.64-8.48 (2H, s), 7.46-7.23 (5H, s), 4.41 (2H, s) 4.21 (1H, s), 3.34 (2H, m), 3.09 (2H, m), 2.18 (2H, m), 1.69 (2H, m).

b) (±)-2-[[5-[(Phenylmethyl)thio]-2-(4-piperidinylamino)thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol

5 Prepared by the method of Example 221, using the product of step a).

MS (APCI) 431 (M+H<sup>+</sup>, 100%).

#### Example 272

10 *N*-[2-[[7-Chloro-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-acetamide

Prepared according to the method of Example 231 using the product of Example 219.

15 MS (APCI) 396, 394 (M+H<sup>+</sup>), 394 (100%).

#### Examples 273-276

Examples 273-276 were prepared by the method of Example 221 using the product of Example 272.

20

#### Example 273

(±)-*N*-[2-[[7-[[1-(Hydroxymethyl)propyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-acetamide

25 MS (APCI) 447 (M+H<sup>+</sup>, 100%)

#### Examples 274

(±)-*N*-[2-[[7-[(2-Hydroxy-1-methylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-acetamide,

30

MS (APCI) 433 ( $M+H^+$ , 100%)

**Examples 275**

*N*-[2-[[7-[(2-Hydroxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-acetamide

MS (APCI) 419 ( $M+H^+$ , 100%)

**Example 276**

*N*-[2-[[7-[[[(1*R*)-1-(Hydroxymethyl)-3-methylbutyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]ethyl]-acetamide,

MS (APCI) 475 ( $M+H^+$ , 100%)

**Example 277**

**7-Chloro-5-[(phenylmethyl)thio]-*N*-[2-(2-thienyl)ethyl]-thiazolo[4,5-*d*]pyrimidin-2-amine**

Prepared by the method of Example 231, using the product of Example 219 and 2-(2-thienyl)ethylamine.

MS (APCI), 420, 418 ( $M+H^+$ ), 418 (100%).

NMR  $\delta$ H ( $d_6$ -DMSO) 7.45-7.32 (5H, m), 6.96 (2H, m), 4.40 (2H, s), 3.78 (2H, s), 3.16 (2H, t).

**Examples 278-284**

Examples 276 to 284 were prepared by the method of Example 221 using the product of Example 277.

**Example 278**

***N*<sup>7</sup>-(2-Methoxyethyl)-5-[(phenylmethyl)thio]-*N*<sup>2</sup>-[2-(2-thienyl)ethyl]thiazolo[4,5-*d*]pyrimidine-2,7-diamine**

5 MS (APCI) 457 (M+H<sup>+</sup>, 100%).

**Example 279**

***N*<sup>7</sup>-(2-Ethoxyethyl)-5-[(phenylmethyl)thio]-*N*<sup>2</sup>-[2-(2-thienyl)ethyl]thiazolo[4,5-*d*]pyrimidine-2,7-diamine**

10

MS (APCI) 471 (M+H<sup>+</sup>, 100%).

**Example 280**

***N*<sup>7</sup>-(2,2-Dimethylpropyl)-5-[(phenylmethyl)thio]-*N*<sup>2</sup>-[2-(2-thienyl)ethyl]thiazolo[4,5-*d*]pyrimidine-2,7-diamine**

15

MS (APCI) 469 (M+H<sup>+</sup>, 100%).

**Example 281**

**(2*R*)-4-Methyl-2-[[5-[(phenylmethyl)thio]-2-[[2-(2-thienyl)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-pentanol**

20

MS (APCI) 499 (M+H<sup>+</sup>, 100%).

**Example 282**

**(±)-1-[[5-[(Phenylmethyl)thio]-2-[[2-(2-thienyl)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-2-propanol**

25

MS (APCI) 457 (M+H<sup>+</sup>, 100%).

30

**Example 283**

(±)-2-[[5-[(Phenylmethyl)thio]-2-[[2-(2-thienyl)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol

5 MS (APCI) 471 (M+H<sup>+</sup>, 100%).

**Example 284**

(±)-2-[[5-[(Phenylmethyl)thio]-2-[[2-(2-thienyl)ethyl]amino]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol

10

MS (APCI) 457 (M+H<sup>+</sup>, 100%).

**Example 285**

2-[[7-Chloro-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-1-ethanol

15

Prepared by the method of Example 231, using the product of Example 219 and 2-aminoethanol.

MS (APCI) 355, 353 (M+H<sup>+</sup>), 353 (100%).

20 NMR δ<sub>H</sub> (d<sub>6</sub>-DMSO) 9.48 (1H, s), 7.45-7.30 (5H, m), 4.95 (1H, t), 4.40 (2H, s), 3.60 (4H, m).

**Examples 286-287**

Examples 286 to 287 were prepared by the method of Example 221 using the product of Example 285.

25

**Example 286**

(2*R*)-2-[[2-[(2-Hydroxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-4-methyl-1-pentanol

30

MS (APCI) 433 ( $M+H^+$ , 100%).

**Example 287**

(±)-*N,N*-Diethyl-1-[2-[(2-hydroxyethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-  
5 *d*]pyrimidin-7-yl]-3-piperidinecarboxamide

MS (APCI) 500 ( $M+H^+$ , 100%).

**Example 288**

10 3-[[7-Chloro-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-1-propanol

Prepared by the method of Example 231, using the product of Example 219 and 3-aminopropanol.

15 MS (APCI) 369, 367 ( $M+H^+$ ), 367 (100%).

NMR  $\delta$ H ( $d_6$ -DMSO) 9.36 (1H, s), 7.43-7.27 (5H, m), 4.57 (1H, t), 4.40 (2H, s), 3.49 (4H, m), 1.75 (2H, m).

**Examples 289-291**

20 Examples 289-291 were prepared by the method of Example 221 using the product of Example 288.

**Example 289**

(2*R*)-2-[[2-[(3-Hydroxypropyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-  
25 *d*]pyrimidin-7-yl]amino]-4-methyl-1-pentanol

MS (APCI) 447 ( $M+H^+$ , 100%).



**Example 290**

(±)-2-[[2-[(3-Hydroxypropyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-butanol

5 MS (APCI) 419 (M+H<sup>+</sup>, 100%).

**Example 291**

(±)-2-[[2-[(3-Hydroxypropyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol

10 MS (APCI) 405 (M+H<sup>+</sup>, 100%)

**Example 292**

2-[[7-Chloro-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-acetamide

15 Prepared by the method of Example 231, using the product of Example 219 and glycineamide hydrochloride.

MS (APCI) 368, 66 (M+H<sup>+</sup>), 366 (100%).

20 NMR δH (d<sub>6</sub>-DMSO) 7.61 (1H, s), 7.45-7.24 (6H, m), 4.40 (2H, s), 4.14-4.12 (2H, m), 9.57 (1H, s).

**Example 293**

2-[[7-[(2-Hydroxy-1-methylethyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]amino]-acetamide

25

Prepared according to the method of Example 221 using the product of Example 292.

MS (APCI) 404 (M+H<sup>+</sup>, 100%).

30

**Example 294****4-[[7-Chloro-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]-3-azetidiny]-1-piperazinesulfonamide**

- 5 Prepared by the method of Example 231, using the product of Example 219 and 3-azetidiny-1-piperazinesulfonamide.

MS (APCI), 512, 514 ( $M+H^+$ ), 512 (100%).

10 NMR  $\delta$ H ( $d_6$ -DMSO) 7.69-7.22 (5H, m), 6.80 (2H, s), 4.40 (2H, s), 4.34-4.12 (4H, m), 3.56-3.50 (1H, m), 3.40 (4H, s), 3.00 (4H, s).

**Example 295****4-[1-[7-[(4-Methylcyclohexyl)amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-2-yl]-3-azetidiny]-1-piperazinesulfonamide,**

- 15 Prepared by the method of Example 221, using the product of Example 294.

MS (APCI) 588 ( $M+H^+$ , 100%).

20 **Example 296**

**7-Chloro-*N*-[[2-(4-morpholinyl)ethyl]-5-[(phenylmethyl)thio]-thiazolo[4,5-*d*]pyrimidin-2-amine**

- 25 Prepared by the method of Example 231, using the product of Example 219 and 2-(4-morpholinyl)ethylamine.

MS (APCI) 424, 422 ( $M+H^+$ ), 422 (100%).

NMR  $\delta$ H ( $d_6$ -DMSO) 9.34 (1H, s), 7.68-7.23 (5H, m), 4.40 (2H, s), 3.59-3.56 (6H, m), 2.54 (2H, t), 2.44-2.41 (4H, m).

**Examples 297-300**

Examples 297-300 were prepared according to the method of Example 221 using the product of Example 296.

**Example 297**

**3-[[2-[[2-(4-Morpholinyl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol**

MS (APCI) 460 ( $M+H^+$ , 100%).

10

**Example 298**

**2-Methyl-2-[[2-[[2-(4-morpholinyl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol**

MS (APCI) 464 ( $M+H^+$ , 100%).

**Example 299**

**(±)-2-[[2-[[2-(4-Morpholinyl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-propanol**

20

MS (APCI) 460 ( $M+H^+$ , 100%).

**Example 300**

**(2*R*)-4-Methyl-2-[[2-[[2-(4-morpholinyl)ethyl]amino]-5-[(phenylmethyl)thio]thiazolo[4,5-*d*]pyrimidin-7-yl]amino]-1-pentanol**

25

MS (APCI) 502 ( $M+H^+$ , 100%).

**Examples 301-302**

Examples 301-302 were prepared by the method of Example 12 using the product of Example 140.

**Example 301**

2-[[2-(3,4-Dihydroxyphenyl)ethyl]amino]-5-[(phenylmethyl)thio]-thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one

MS (APCI) 427 (M+H<sup>+</sup>, 100%).

**Example 302**

(±)-2-[(2-Hydroxy-1-methylethyl)amino]-5-[(phenylmethyl)thio]-thiazolo[4,5-*d*]pyrimidin-7(4*H*)-one

MS (APCI) 349 (M+H<sup>+</sup>, 100%).

**Pharmacological Data****Ligand Binding Assay**

[<sup>125</sup>I]IL-8 (human, recombinant) was purchased from Amersham, U.K. with a specific activity of 2,000Ci/mmol. All other chemicals were of analytical grade. High levels of hrCXCR2 were expressed in HEK 293 cells (human embryo kidney 293 cells ECACC No. 85120602) (Lee *et al.* (1992) *J. Biol. Chem.* **267** pp16283-16291). hrCXCR2 cDNA was amplified and cloned from human neutrophil mRNA. The DNA was cloned into PCRScript (Stratagene) and clones were identified using DNA. The coding sequence was sub-cloned into the eukaryotic expression vector RccMV (Invitrogen). Plasmid DNA was prepared using Quiagen Megaprep 2500 and transfected into HEK 293 cells using Lipofectamine reagent (Gibco BRL). Cells of the highest expressing clone were harvested in phosphate-buffered saline containing 0.2%(w/v) ethylenediaminetetraacetic acid (EDTA) and centrifuged (200g, 5min.). The cell pellet was resuspended in ice cold homogenisation

buffer [10mM HEPES (pH 7.4), 1mM dithiothreitol, 1mM EDTA and a panel of protease inhibitors (1mM phenyl methyl sulphonyl fluoride, 2µg/ml soybean trypsin inhibitor, 3mM benzamidine, 0.5µg/ml leupeptin and 100µg/ml bacitracin)] and the cells left to swell for 10 minutes. The cell preparation was disrupted using a hand held glass mortar/PTFE pestle homogeniser and cell membranes harvested by centrifugation (45 minutes, 100,000g, 4°C). The membrane preparation was stored at -70°C in homogenisation buffer supplemented with Tyrode's salt solution (137mM NaCl, 2.7mM KCl, 0.4mM NaH<sub>2</sub>PO<sub>4</sub>), 0.1%(w/v) gelatin and 10%(v/v) glycerol.

All assays were performed in a 96-well MultiScreen 0.45µm filtration plates (Millipore, U.K.). Each assay contained ~50pM [<sup>125</sup>I]IL-8 and membranes (equivalent to ~200,000 cells) in assay buffer [Tyrode's salt solution supplemented with 10mM HEPES (pH 7.4), 1.8mM CaCl<sub>2</sub>, 1mM MgCl<sub>2</sub>, 0.125mg/ml bacitracin and 0.1%(w/v) gelatin]. In addition, a compound of formula (I) according to the Examples was pre-dissolved in DMSO and added to reach a final concentration of 1%(v/v) DMSO. The assay was initiated with the addition of membranes and after 1.5 hours at room temperature the membranes were harvested by filtration using a Millipore MultiScreen vacuum manifold and washed twice with assay buffer (without bacitracin). The backing plate was removed from the MultiScreen plate assembly, the filters dried at room temperature, punched out and then counted on a Cobra γ-counter.

The compounds of formula (I) according to the Examples were found to have IC<sub>50</sub> values of less than (<) 10µM.

#### **Intracellular Calcium Mobilisation Assay**

Human neutrophils were prepared from EDTA-treated peripheral blood, as previously described (Baly *et al.* (1997) *Methods in Enzymology* 287 pp70-72), in storage buffer [Tyrode's salt solution (137mM NaCl, 2.7mM KCl, 0.4mM NaH<sub>2</sub>PO<sub>4</sub>) supplemented with 5.7mM glucose and 10mM HEPES (pH 7.4)].

The chemokine GRO $\alpha$  (human, recombinant) was purchased from R&D Systems (Abingdon, U.K.). All other chemicals were of analytical grade. Changes in intracellular free calcium were measured fluorometrically by loading neutrophils with the calcium sensitive fluorescent dye, fluo-3, as described previously (Merritt *et al.* (1990) *Biochem. J.* 269, pp513-519). Cells were loaded for 1 hour at 37°C in loading buffer (storage buffer with 0.1%(w/v) gelatin) containing 5 $\mu$ M fluo-3 AM ester, washed with loading buffer and then resuspended in Tyrode's salt solution supplemented with 5.7mM glucose, 0.1%(w/v) bovine serum albumin (BSA), 1.8mM CaCl<sub>2</sub> and 1mM MgCl<sub>2</sub>. The cells were pipetted into black walled, clear bottom, 96 well micro plates (Costar, Boston, U.S.A.) and centrifuged (200g, 5 minutes, room temperature).

A compound of formula (I) according to the Examples was pre-dissolved in DMSO and added to a final concentration of 0.1%(v/v) DMSO. Assays were initiated by the addition of an A<sub>50</sub> concentration of GRO $\alpha$  and the transient increase in fluo-3 fluorescence ( $\lambda_{Ex}$  =490nm and  $\lambda_{Em}$  = 520nm) monitored using a FLIPR (Fluorometric Imaging Plate Reader, Molecular Devices, Sunnyvale, U.S.A.).

The compounds of formula (I) according to the Examples were tested and found to be antagonists of the CXCR2 receptor in human neutrophils.